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PHYSIOLOGIC CONSIDERATIONS IN THE TREATMENT OF PORTAL CIRRHOSIS

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The main clinical characteristics of portal cirrhosis are well known. It is most frequently seen during the fifth and sixth decades, the average age being close to 50 years (table 1). Men are more frequently affected than women, the proportion being approximately three to one. The results of a study of 108 cases seen at the New York Post-Graduate Hospital (table 2) were very similar to those reported recently from New York by Patek and Ratnoff,[1] by Fleming and Snell[2] at the Mayo Clinic and by Wayburn and Guerard[3] from San Francisco. These studies in turn do not differ greatly from the earlier reports of Wickham Legg,[4] Murchison[5] and Rolleston.[6]

Clinical studies regarding the pathogenesis of this condition are equivocal. The history of the abuse of alcohol is a frequent but not essential finding. Syphilis was present in about one sixth of the cases reported. This is a much smaller proportion than that noted in some of the earlier studies. Rolleston[6] in the first edition of his classic work reported that syphilis was considered to give rise to lesions quite different from those of portal cirrhosis. In the last edition,[7] published twenty-four years later, he quotes various authors as finding a positive Wassermann reaction in from 40 to 80 per cent of cirrhotic patients.

Clinical evidence as to the pathogenesis of cirrhosis is not as conclusive as is some of the experimental evidence. The older literature has been reviewed by Moon,[8] who points out that numerous agents, diverse in character, are capable of causing degeneration and necrosis of hepatic cells. The continued or repeated action of these agents results in the production of chronic diffuse hepatitis as indicated by degeneration and necrosis, parenchymal regeneration and proliferation of fibrous tissue.

A few agents,[9] including the chlorinated hydrocarbons, especially chloroform and carbon tetrachloride, inorganic poisons such as phosphorus, arsenic and selenium,[10] other chemical compounds, especially the tars, and some bacterial infections, are accepted on both clinical and experimental grounds as capable of producing cirrhotic changes in the liver.

The role of alcohol is still indeterminate. Connor[11] in particular has emphasized the importance of the fatty infiltration of the liver so frequently noted in alcoholic addicts especially when the excessive intake of alcohol is associated with an insufficient diet. Prolonged fatty infiltration of the liver gradually produces a progressive perilobular fibrosis and eventually a true portal cirrhosis.

This literature dealing with the relation of the liver to fat metabolism has been reviewed recently by several authors.[12] Many different factors acting either singly or in combination may produce an increase in the amount of fat in the liver. A high fat diet, for example, will produce a permanent increase in contrast to the temporary increase produced by fasting. The chronic fatty infiltration of the liver reported in pancreatectomized dogs and some patients with diabetes is well recognized. Extracts of the anterior pituitary will produce a fatty liver. It is generally accepted that an undue increase in the amount of fat present in the liver will contribute to the development of cirrhosis.

Conversely, an increase in the amount of protein or carbohydrate in the diet usually decreases the amount of fat in the liver. Choline, pancreatic extract or lipocaic will prevent the accumulation of fat due to a high fat diet and so prevent the development of cirrhosis.

Evidence is being accumulated that dietary factors other than the relative amounts of carbohydrate, protein and fat in the diet affect the liver. György and Goldblatt[13] observed that when young rats were kept on a diet devoid of vitamin B but supplemented with thiamine, riboflavin and pyridoxine they showed evidence of hepatic injury. This consisted primarily of

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8. Moon, V. H.: Experimental Cirrhosis in Relation to Human Cirrhosis, Arch. Path. **18**: 380 (Sept.) 1934.
9. Greene, C. H.: Liver and Biliary Tract: A Review for 1941, Arch. Int. Med. **69**: 691-714 (April) 1942.
10. Smith, M. I.: Chronic Endemic Selenium Poisoning: A Review of the More Recent Field and Experimental Studies, J. A. M. A. **116**: 562 (Feb. 15) 1941.
11. Connor, C. L.: Fatty Infiltration of the Liver and the Development of Cirrhosis in Diabetes and Chronic Alcoholism, Am. J. Path. **14**: 347 (May) 1938; The Etiology and Pathogenesis of Alcoholic Cirrhosis of the Liver, J. A. M. A. **112**: 387 (Feb. 4) 1939.
12. Greene, C. H., and Hotz, Richard: Liver and Biliary Tract: A Review for 1939, Arch. Int. Med. **63**: 778-808 (April) 1939. Greene, C. H.; Handelsman, M. B., and Babey, A. M.: Liver and Biliary Tract: A Review for 1936, ibid. **59**: 724 (April) 1937. Best, C. H., and Ridout, J. H.: Choline as a Dietary Factor, in Luck, J. M., and Smith, J. H. C.: Annual Review of Biochemistry, Stanford University, Calif. **8**: 439, 1939. Channon, J. H.: Fat Metabolism, in Luck and Smith, ibid. **9**: 231, 1940.
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acute diffuse necrosis with fatty infiltration. In some instances considerable periportal fibrosis was observed. Rats fed on the same basal diet supplemented with yeast or yeast extract did not show pathologic changes in the liver. Shortly afterward, Rich and Hamilton [14] reported the development of cirrhosis of the liver on a nutritional basis in rats, while Spellberg, Keeton and Ginsberg [15] made similar observations in guinea pigs. In both studies the addition of yeast to the diet prevented the development of the changes in the liver. The earlier studies of Curtis and Newburgh [16] and others had shown that an excess of cystine in the diet would produce acute hepatic necrosis. Studies by György, Poling and Goldblatt [17] and Blumberg and McCollum [18] showed that the addition of extra cystine to the experimental diet of rats accentuated the development of cirrhosis. Yeast or choline prevented the cirrhosis even though extra cystine was fed. Similar results are reported by Lillie, Daft and Sebrell,[19] who produced cirrhosis in rats by the use of a diet low in protein and fat with added cystine. The cirrhosis was prevented by feeding choline, methionine or casein either singly or in combination. Supplying 20 per cent alcohol to the rats in place of drinking water apparently had no influence on the results.

TABLE 1.—*Incidence of Portal Cirrhosis with Age*

Age	N. Y. P. G. H. Series	Mayo Clinic [2] Series	Total
0- 9	0	0	0
10-19	0	3	3
20-29	7	11	18
30-39	16	25	41
40-49	38	56	94
50-59	28	68	96
60-69	19	29	48
70-79	0	8	8
Total	108	200	308
Average age	48.3	50.4	49.2
Per cent:			
Males	78	75	76
Females	22	25	24

Not only may cirrhosis of the liver be produced in experimental animals by dietary means but it has been shown that dietary deficiencies render the liver more susceptible to the effects of various toxic substances.[20]

Closely related to the studies of the production of cirrhotic changes in the liver by dietary means are the studies of the effects of diet on the production of experimental cancer of the liver. It is now known that many chemical compounds have carcinogenic properties.[21] The first changes in the liver of a rat on this carcinogenic regimen are necrosis and fibrosis suggestive of cirrhosis. The characteristic hepatoma develops later. Deficient diets similar to those producing cirrhosis render the animals more susceptible to cancer of the liver.[22] The addition of dried liver, yeast, riboflavin and casein, methionine or choline to the diet, on the other hand, has a protective action.

While the experimental production of cirrhosis of the liver by dietary means now is an accepted fact, the factors responsible are still a source of debate. Many of the diets produce a fatty infiltration of the liver, and the cirrhosis has been ascribed to this. The protective action of choline is cited as confirmatory evidence for this view. On the other hand, the liver is concerned in the absorption, storage and utilization of the various vitamins. Rhoads has stressed the importance of the vitamins, especially those of the B complex, for the maintenance of normal structure and function of the hepatic parenchyme. Supplementing deficient diets by casein, yeast and liver or their extracts had a protective effect. The role of vitamin deficiency in the production of cirrhosis, therefore, has been stressed.

The relative importance of these two factors of excess fat and vitamin deficiency in the production of cirrhosis is not established at the present time, but their importance in treatment has been established.

Goodhart and Jolliffe [23] administered large doses of vitamin B to a series of alcoholic polyneuritis patients with good results. Several of the patients had hepatic cirrhosis, and they noted a coincident improvement in the general condition of the patient as well as of the polyneuritis. Patek and Wayburn and Guerard also reported small series of cases showing improvement on vitamin therapy.

More extensive studies have been reported by Patek and Post and by Fleming and Snell. The former used a diet of protein 139, fat 175 and carbohydrate 365 Gm. with a caloric intake of 3,591. Fifty Gm. of powdered brewers' yeast daily was included in the diet. In addition to the yeast, the patients received intramuscular injections of concentrated liver extract 5 cc. twice weekly and of 5 mg. of thiamine hydrochloride daily.

Fleming and Snell used a diet of from 350 to 500 Gm. of carbohydrate, 110 Gm. of protein and approximately 50 Gm. of fat. The protein was chiefly of vegetable origin or derived from milk or egg white. This diet was supplemented by various vitamin preparations such as 30 minims (2 cc.) of oleum percomorphum and 9 to 12 ounces (265 to 355 cc.) of orange juice or 100 mg. of ascorbic acid daily. Liver extract was given either by mouth, 2 ounces (60 cc.) daily or 2 cc. of a liver extract intramuscularly three times a week. Thiamine hydrochloride, 4 to 10 mg. daily, and two to four tablets of brewers' yeast were given with each meal.

14. Rich, A. R., and Hamilton, J. D.: The Experimental Production of Cirrhosis of the Liver by Means of a Deficient Diet, Bull. Johns Hopkins Hosp. **66**: 185 (March) 1940.

15. Spellberg, M. A., and Keeton, R. W.: The Production of Fatty and Fibrotic Livers in Guinea Pigs and Rabbits by Seemingly Adequate Diets, Am. J. M. Sc. **200**: 688 (Nov.) 1940. Spellberg, M. A.; Keeton, R. W., and Ginsberg, Robert: Dietary Production of Hepatic Cirrhosis in Rabbits with an Analysis of the Factors Involved, Arch. Path. **33**: 204 (Feb.) 1942.

16. Curtis, A. C., and Newburgh, L. H.: The Toxic Action of Cystine on the Liver of the Albino Rat, Arch. Int. Med. **39**: 828 (June) 1927. Sullivan, M. X.; Hess, W. C., and Sebrell, W. H.: Studies on Biochemistry of Sulfur: Preliminary Studies on Amino Acid Toxicity and Amino Acid Balance, Pub. Health Rep. **47**: 75 (Jan. 8) 1932. Lillie, R. D.: Histopathological Changes Produced in Rats by Addition to Diet of Various Amino Acids (Glycine, Lysine, Tryptophan, Cystine, Tyrosine and Glutamic Acid) and of Mixtures of Some of Them, ibid. **47**: 83 (Jan. 8) 1932. Earle, D. P., Jr., and Victor, Joseph: Cirrhosis of the Liver Caused by Excess Dietary Cystine, J. Exper. Med. **73**: 161 (Feb.) 1941.

17. György, Paul; Poling, C. E., and Goldblatt, Harry: Necrosis, Cirrhosis and Cancer of the Liver in Rats Fed a Diet Containing Dimethylaminoazobenzene, Proc. Soc. Exper. Biol. & Med. **47**: 41 (June) 1941.

18. Blumberg, Harold, and McCollum, E. V.: The Prevention by Choline of Liver Cirrhosis in Rats on High Fat, Low Protein Diets, Science **93**: 598 (June 20) 1941. Webster, G. T.: Cirrhosis of the Liver Among Rats Receiving Diets Poor in Protein and Rich in Fat, J. Clin. Investigation **21**: 385 (July) 1942.

19. Lillie, R. D.; Daft, F. S., and Sebrell, W. H. Jr.: Cirrhosis of the Liver in Rats on a Deficient Diet and the Effect of Alcohol, Pub. Health Rep. **56**: 1255 (June 13) 1941. Daft, F. S.; Sebrell, W. H. Jr., and Lillie, R. D.: Production and Apparent Prevention of a Dietary Liver Cirrhosis in Rats, Proc. Soc. Exper. Biol. & Med. **48**: 228 (Oct.) 1941.

20. Messinger, W. J., and Hawkins, W. B.: Arsphenamine Liver Injury Modified by Diet: Protein and Carbohydrate Protective but Fat Injurious, Am. J. M. Sc. **199**: 216 (Feb.) 1940. von Glahn, W. C.; Flinn, F. B., and Keim, W. F., Jr.: Effect of Certain Arsenates on the Liver, Arch. Path. **25**: 488 (April) 1938. von Glahn, W. C., and Flinn, F. B.: The Effect of Yeast on the Incidence of Cirrhosis Produced by Lead Arsenate, Am. J. Path. **15**: 771 (Nov.) 1939.

21. Kinosita, Riojun: Studies on the Cancerogenic Azo and Related Compounds, Yale J. Biol. & Med. **12**: 287 (Jan.) 1940.

22. Rhoads, C. P.: Recent Studies in the Production of Cancer by Chemical Compounds: The Conditioned Deficiency as a Mechanism, Bull. New York Acad. Med. **18**: 53 (Jan.) 1942.

23. Goodhart, Robert, and Jolliffe, Norman: Effects of Vitamin (B_1) Therapy on the Polyneuritis of Alcohol Addicts, J. A. M. A. **110**: 414-418 (Feb. 5) 1938.

While differing greatly in detail, the diets used by these two sets of investigators were alike in that they were high protein, high vitamin, high caloric diets. The protein was preponderately vegetable or of dairy origin. Patek and Post do not stress the point, but in their diet less than one fourth of the protein was supplied by meat. Yeast and liver extracts were used to insure an adequate supply of vitamins.

Both Patek and Post and Fleming and Snell report encouraging results in their series of cases. Not only was the clinical course of the disease influenced favorably but there was an increased period of survival in the treated groups of cases as compared to the control groups. It would seem, therefore, that a high protein, high vitamin diet is capable of favorably influencing the course of a portal cirrhosis presumably by favoring regenerative processes in the hepatic parenchyma. The reports are agreed that on such a diet many of these patients show slow but progressive improvement with the disappearance of ascites, gain in weight, strength and appetite and increase in serum proteins. The results are encouraging, but it must be remembered that the effects are slow. It takes time for the improvement in nutrition as well as for the regeneration of hepatic tissue to take place. Patek reports two months on the average before definite improvement becomes apparent. Fleming and Snell reported that there was very little difference between the mortality rates for the control and treated groups of cases during the first year.

The dietary treatment of patients with cirrhosis, therefore, represents only one phase of management of this condition. The typical patient reports to the physician with a distended abdomen, palpable spleen, dilated veins of the abdomen and considerable amount of ascitic fluid. It is frequently the discomfort produced by the latter that makes him demand systemic relief. This clinical picture, which is also described as the syndrome of portal hypertension, is well known. Two factors enter into this syndrome particularly with reference to the production of ascites. On the one hand there is the interference with the blood flow through the liver [24] as emphasized by Herrick,[25] McIndoe,[26] Wakim and Mann [27] and others. The presence of portal hypertension has been confirmed at operation by direct measurements of the portal pressure.[28] Because of the development of collateral circulation and so-called caput medusae in cases of cirrhosis, an attempt was made to study the venous pressure directly in the veins of the abdominal wall to see how far it reflects the portal pressure. It has been our experience that the venous pressure in the veins of the abdominal wall of patients with cirrhosis is higher than that in the antecubital veins of the same patient. However, following paracentesis the veins in the abdominal wall collapse and further studies were not possible, so that one must conclude that ascites produces a measure of interference with the venous flow in the abdominal wall. The venous dilatation, therefore, is not necessarily evidence of development of collateral circulation.

Portal hypertension is only one factor in the development of ascites. Another factor is hypoproteinemia, particularly diminution in the albumin fraction of the serum in consequence of damage to the liver. It is now accepted that the more advanced the cirrhosis, the greater the chance of the patient having a reduction in the serum albumin. In severe involvement there is not only a reduction in the albumin but also a reversal of the albumin/globulin ratio. It is this change in the serum proteins which is responsible for the diagnostic value of the Takata-Ara test in cirrhosis. In addition to the reduction of serum protein there may also be changes in the osmotic pressure of the serum proteins, as suggested by Butt, Snell and Keys.[29]

In the early stages of cirrhosis, ascites often is readily controlled by the use of mercurial diuretics especially when used with ammonium chloride or nitrate. In my experience the efficiency of the mercurial diuretics apparently varies with the difference between the protein concentration of the blood plasma and that of the ascitic fluid. The more advanced the cirrhosis

TABLE 2.—*Clinical Picture of Portal Cirrhosis*

	N. Y. P. G. H.	Mayo Clinic [2]	Patek and Post [1]	Ratnoff and Patek [1]	Wayburn [3]
Total number of cases	108	200	54	386	272
Average age	48.3	50.4	50.3	50	..
Sex: Male, per cent	78	75	65	69	58
Female, per cent	22	25	35	31	42
Antecedent factors					
Alcohol	38	51	87	54	72
Malnutrition	..	..	81	17	23
Syphilis	17	16	26	16	..
Arsphenamine	6	..	20	9	..
Not determined	33	38.5	..	..	..
Symptoms					
Abdominal swelling	72	97	89	80	..
Edema	..	58	85	61	..
Loss of weight	38	58.5	78	53	..
Dyspepsia	34	30	54	33	..
Hematemesis	15	13.5	24	27	35
Pain	21	46	40	31	..
Clinical signs					
Ascites	74	97	89	80	64
Palpable liver	84	54.5	81	75	74
Palpable spleen	27	31.5	70	44	..
Jaundice	30	45.5	61	65	58
Collateral veins	28	34	76	23	..
Anemia	71	..	40	..	48

and the greater the reduction in the serum proteins, therefore, the less effective has been the response to mercurial diuretics.

Anemia frequently is present in cirrhosis. Under these conditions transfusion improves the general condition of the patient not only by combating the anemia but also by increasing the serum protein, which improves the response to the mercurial diuretics.

Paracentesis has long been recognized as the method of last resort in the control of ascites. When the hepatic damage is so pronounced that the ascites can be controlled only by repeated and frequent paracenteses, the patient tends to go down hill rapidly. Hale-White [30] was one of the first to suggest the serious prognostic import of paracentesis. It is true that some investigators have argued that paracentesis is without effect [31] on the serum proteins or on the process of protein synthesis, though this is denied by Benedetti.[32]

24. Greene, C. H.; Plotz, Milton, and Localio, S. A.: Liver and Biliary Tract: A Review for 1937, Arch. Int. Med. **61:** 655 (April) 1938.

25. Herrick, F. C.: An Experimental Study into the Cause of the Increased Portal Pressure in Portal Cirrhosis, J. Exper. Med. **9:** 93, 1907.

26. McIndoe, A. H.: Vascular Lesions of Portal Cirrhosis, Arch. Path. & Lab. Med. **5:** 23-42 (Jan.) 1928.

27. Wakim, K. G., and Mann, F. C.: Effect of Experimental Cirrhosis on the Intrahepatic Circulation of Blood in the Intact Animal, Arch. Path. **33:** 198 (Feb.) 1942.

28. Thompson, W. P.; Caughey, J. L.; Whipple, A. O., and Rousselot, L. M.: Splenic Vein Pressure in Congestive Splenomegaly (Banti's Syndrome).

29. Butt, H. R.; Snell, A. M., and Keys, Ancel: Plasma Proteins in Hepatic Disease: A Study of the Colloid Osmotic Pressure of Blood Serum and of Ascitic Fluid in Various Diseases of the Liver, Arch. Int. Med. **63:** 143-155 (Jan.) 1939.

30. Hale-White, W.: The Cause and Prognosis of Ascites Due to Alcoholic Cirrhosis of the Liver, to Perihepatitis and to Chronic Peritonitis, Guy's Hosp. Rep. **49:** 1-42, 1892.

31. Miacoli, D., and Ferroni, M.: Protein Picture of Blood and Ascitic Fluid in Atrophic Cirrhosis of the Liver, Rassegna di fisiopatol. **12:** 193 (May) 1940.

32. Benedetti, G.: Modification of Equilibrium of Blood Proteins After Paracentesis in Liver Cirrhosis, Rassegna di fisiopatol. **10:** 159 (March) 1938.

Recent studies of Post and Patek [33] suggest that protein synthesis, particularly that of serum albumin, is more difficult for the damaged liver than for the normal one. When the protein content of ascitic fluid is under 1 per cent, considerable amounts can be removed without much gross loss of protein. On the other hand, tapping 3,000 cc. containing 2 per cent of protein would make a loss of 60 Gm. of protein, which is an appreciable quantity. We have tried in a few instances to prevent protein depletion through paracentesis by concentrating the ascitic fluid and reinjecting the concentrated protein solution intravenously. Severe reactions were encountered, and treatment did not prove to be practicable. Numerous investigators have shown the value of plasma infusions in correcting a deficiency of serum protein in a variety of conditions. Ascitic fluid, chemically, is very similar if not the same as serum, and it has been advocated for the treatment of shock.[34] We therefore tried paracentesis and the direct readministration of ascitic fluid. The results have been encouraging.

REPORT OF CASES

CASE 1.—A machinist aged 61, first seen on Feb. 5, 1939, had been a consistent alcoholic addict for many years. His father died of cirrhosis of the liver. Abdominal distention and epigastric distress were first noted about a month before admission.

Examination showed evidence of a moderate degree of malnutrition. The abdomen was considerably distended, with evidence of fluid. The superficial abdominal veins were distended. Hemorrhoids were present. Vascular spiders were noted on the chest. The liver was palpated 3 cm. below the costal margin and was hard and slightly irregular. There was pitting edema of the ankles.

TABLE 3.—*Clinical Response to Infusion of Ascitic Fluid in Case 1.*

Date	Weight, Pounds	Paracentesis, Cc.	Infusion of Ascitic Fluid, Cc.	Fluid Intake, Cc.	Urinary Output, Cc.	Excess of Urinary Output, Cc.
5/ 9	154	300	200	1,000	600	.....
10	...	300	300	880	500	.....
11	...	500	500	1,320	830	.....
12	...	600	600	1,520	750	.....
13	...	700	700	1,560	1,340	.....
14	149	...	...	900	2,450	1,550
15	...	800	800	1,640	1,500	.....
16	145	...	...	860	2,240	1,580
17	143	...	...	900	1,440	640
18	142½	...	...	1,020	1,150	130
19	140¾	1,000	1,000	1,060	1,230	.....
20	138½	...	...	1,020	1,970	950
21	137½	...	...	960	1,240	280
22	136½	...	...	900	1,010	110
23	137	...	...	1,000	1,470	420
24	...	...	...	960	1,220	260
25	137½	...	...	1,260	1,110	...
26	137½	...	...	840	1,030	...
27	137½	...	...	1,200	930	...
28	139½	1,000	1,000	960	1,575	615
29	138	...	...	1,200	1,040	...
30	...	...	...	960	910	...
31	136	...	...	750	1,400	650
6/ 1	135	...	...	900	845	...
Total.....			5,100			7,185

The Wassermann reaction was positive. The urinalysis and blood counts were normal. The bromsulphalein test showed retention at thirty minutes. The Takata-Ara test was positive. An esophageal roentgenogram showed small varices in the lower portion of the esophagus.

He was placed on a high carbohydrate high vitamin diet with a restricted intake of salt. Ammonium chloride and potassium nitrate were given in addition. During the next two months he was given nine injections of 1 cc. each of either salyrgan-theophylline or of mercupurin without diuretic response. Nineteen days after admission a paracentesis of 3,750 cc. was necessary, and four weeks later 24,000 cc. was withdrawn.

TABLE 4.—*Changes in Serum Protein in Case 1*

Date	Serum Protein			Ascitic Fluid
	Total	Albumin	Globulin	Total Protein
2/ 6/39.....	5.5	...	...	...
2/23/39.....	6.0	1.4	4.6	...
4/14/39.....	6.8	2.9	3.9	1.8
5/ 8/39.....	8.0	4.0	4.0	...
5/19/39.....	8.5	4.7	3.8	3.9
6/ 1/42.....	6.9	3.2	3.7	...

He was discharged from the hospital after this paracentesis but returned three weeks later and 17,000 cc. was removed. Infusions of ascitic fluid were then started. During the following three weeks 5,100 cc. of ascitic fluid containing over 150 Gm. of protein was given intravenously. During this period the urinary output exceeded the fluid intake by 7,185 cc., and he lost 19 pounds (8.6 Kg.). At the time of discharge from the hospital, June 1, 1939, he was free from ascites. The serum proteins were 8.5 per cent. Three years later, June 1, 1942, he was well, and the liver was large and firm 3 cm. below the costal margin. The spleen was just palpable. The veins over the abdominal wall were not unduly prominent. There was no ascites. The serum proteins were 6.9 per cent.

CASE 2.—A junk dealer aged 30 first came to the hospital in March 1941 because of flatulent indigestion. He had been decidedly alcoholic for many years. He was underweight and showed evidences of malnutrition. The abdomen was moderately distended, but no fluid was present. The spleen could not be felt, but the liver came down to the umbilicus. He left the hospital against advice the following day. In July frequent nosebleeds began and he noted an icteric tint to his sclera. He returned to the hospital in November with a slight icterus and pronounced ascites. Other findings were the same as before. The icterus quickly disappeared but the ascites increased progressively. The response to mercurial diuretics was unsatisfactory. On December 17 a paracentesis of 9,200 cc. was done. Following the paracentesis there was a copious extravasation of fluid into the scrotum and back up to the axilla. This gradually was absorbed. Reinfusion of ascitic fluid was then started without outward reaction. On Jan. 13, 1942, a second paracentesis of 6,000 cc. was necessary. In the following seven days he received 4,175 cc. of ascitic fluid containing 138 Gm. of protein intravenously. His weight dropped from 162 pounds (73.5 Kg.) on December 23 to 144 pounds (65 Kg.) on discharge. The serum proteins were albumin 2.8, globulin 4.2, total protein 7.0 on admission and albumin 3.7, globulin 4.7, total protein 8.4 on discharge.

He has reported continued health and freedom from ascites since discharge but refused any further laboratory study.

COMMENT

In some instances, as indicated by cases 1 and 2, large amounts of ascitic fluid have been injected intravenously and the protein apparently has been retained in the blood stream. Following the injections there has been an increase in the serum protein level. As the serum protein level increased, a spontaneous diuresis was observed with complete reabsorption of the remaining ascites. Clinically, improvement in these cases was maintained for a considerable period after the completion of the series of injections.

The biggest difficulty has been the matter of reactions. They seem to be more frequent if the ascitic fluid is injected immediately after tapping. The paracentesis is done under sterile conditions and the fluid

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34. Davis, H. A., and Blalock, J. E., Jr.: Autologous and Homologous Transfusions of Human Ascitic Fluid, J. Clin. Investigation **18**: 219-224 (March) 1939.

is saved in transfusion bottles, which are kept in the ice box, where cells and bits of fibrin are allowed to settle out. Sterility is confirmed by cultures and the protein content is determined. After twenty-four to seventy-two hours the clear fluid is siphoned off and given intravenously. The infusion is made at room temperature. For the most part it has been given in amounts of 500 to 1,000 cc. a day rather than as larger single injections. When these precautions are observed, reactions have been infrequent, though an occasional slight chill has been noted. When the ascitic fluid has been very dilute with less than 1 per cent of protein, the amount of protein lost has not been sufficient to warrant its reinjection. However, if the ascitic fluid contains more than 1 per cent of protein, this procedure has been used. A satisfactory response has not been obtained in all cases. The exact details for the handling of the ascitic fluid have not been completely established, but, in selected cases when the protein concentration of the fluid is high and the serum proteins are reduced, I believe that this method of conserving protein is of value in the management of ascites.

Not only is anemia present in cases of cirrhosis, but in the more severe cases this anemia is of the hyperchromic macrocytic type and the blood picture is not unlike that seen in pernicious anemia. This is due to the fact that the damaged liver is no longer able to store the antianemic fraction of the food. In these cases the blood count can be improved and the anemia controlled in part by the intramuscular use of large doses of liver extract just as in cases of pernicious anemia.

The patient with cirrhosis frequently shows a reduction in the prothrombin time of the blood which, if pronounced, will cause a tendency to hemorrhage. The prothrombin time of the blood of a patient with cirrhosis, therefore, should be watched and sufficient vitamin K administered to keep this at a normal level. In the more severe cases of cirrhosis this may not be possible because the severely damaged liver is unable to form prothrombin even though an adequate supply of vitamin K is present.

The most serious hemorrhages in cases of portal cirrhosis usually are due to ruptured esophageal varices. Many different methods have been tried to reduce the portal flow or obliterate the varices with varying degrees of success—splenectomy used by W. J. Mayo [35] and ligation of the coronary vein of the stomach alone as described by Walters [36] or combined with the ingestion of sodium morrhuate into the intra-abdominal vessels as used by Grace.[37] Most recently Crafoord and Frenckner [38] and Moersch [39] has brilliantly demonstrated the possibility of the direct injection of the esophageal varices.

The most discussed surgical procedure in the treatment of cirrhosis has been the operation of omentopexy, which usually bears the names of Talwa and Morrison. The consensus at present is that the results of operation as used in the past have been most unsatisfactory. At the same time a considerable number of cases have been reported in which there was freedom from ascites, with good health, five to twenty years afterward. This would suggest that the results depend in part on the type of cases selected for operation. I have seen a few cases in which apparently great benefit resulted from omentopexy. In some of these cases operation was performed before ascites developed. In others the continuance of ascites required paracentesis at frequent intervals. After six months to a year evidence of abdominal collaterals developed and ascites gradually cleared up. A considerable interval of time would seem to be necessary before the benefits of omentopexy can be expected to develop. As a last hope, after other methods of treatment have failed, omentopexy would not seem to be indicated. Final conclusions as to its value cannot be drawn until a series of cases have been reported in which the operation was done early in the disease and enough time had elapsed for a collateral circulation, sufficient to relieve the portal hypertension, to develop. Even in such a series of cases the interpretation of results would be difficult, for the longer period of survival would also permit regenerative changes in the liver.

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SUMMARY

Recent experimental studies have shown that cirrhosis of the liver can be produced in animals by dietary means. Fatty infiltration of the liver and vitamin deficiencies both play a role in the development of this cirrhosis.

Clinical evidence based in part on these experimental studies indicates the value of high protein, high vitamin diets in the treatment of patients with portal cirrhosis.

In selected cases, infusions of ascitic fluid seem to have some value in conserving blood protein and treating hypoproteinemia.

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ABSTRACT OF DISCUSSION

DR. SEYMOUR J. GRAY, Chicago: I was particularly interested in Dr. Greene's remarks on hypoproteinemia. Electrophoretic analyses of the serum proteins in various liver diseases indicate that two or more protein fractions are abnormal in every case. The most characteristic alteration of the serum proteins in liver disease is a large increase in gamma globulin and a decrease in serum albumin. These changes are seen most frequently and to the greatest degree in cirrhosis of the liver and next most frequently in the acute parenchymatous diseases. Although the serum globulin or albumin globulin ratio is not infrequently normal on chemical analysis in the acute parenchymatous diseases of the liver, the qualitative distribution of the alpha, beta and gamma globulins electrophoretically is invariably abnormal. Thus the qualitative distribution of the serum globulin fractions may be definitely abnormal electrophoretically in spite of a quantitatively normal serum globulin or albumin globulin ratio. Significant increases in beta globulin were observed in all types of liver disease but to a considerably less degree and frequency than the gamma globulin changes. Abnormalities of the serum proteins electrophoretically are less prominent in metastatic carcinoma of the liver than in any other form of liver disease. Jaundice alone does not produce any significant serum protein changes on electrophoretic analysis. The diseased liver, according to our studies, appears to produce the largest molecular weight protein fractions more readily than the smaller molecular weight fractions. This may be explained by Whipple's theory that protein is stored in the liver as complex protein aggregates which are broken down by the liver to supply the serum and tissue proteins as they are needed. This "intermediate protein" is converted into gamma globulin by the

diseased liver more readily than into the smaller protein fractions as alpha globulin and albumin. Finally, our studies indicate that the serum protein changes in liver disease result primarily from the inability of the liver to produce normal serum proteins rather than from external loss in the ascitic fluid.

Dr. W. B. Yegge, Denver: I heard several members of the audience say that Dr. Greene had not mentioned what he thought about bile salts in the treatment of cirrhosis. You must remember Dr. Greene's paper had to do with portal cirrhosis, and portal cirrhosis and biliary cirrhosis are two separate things. Bile salts are more often used in biliary cirrhosis. There are different types of bile salts, and some of them are used for biliary drainage and others for liver cell stimulation. This brings up one thing of which I hope the Council on Pharmacy and Chemistry will take note, and that is that there should be some way in which these drugs could be labeled so we would know with what we are dealing. I should like to have a label put on each drug showing exactly what it contains so that the practicing physician would know what he is using. It is annoying to be educated by detail men who know only what some one has told them about a particular drug.

Dr. Wallace M. Yater, Washington, D. C.: I should like to bring up the point of the great difficulty of early diagnosis in most cases of cirrhosis. If we could diagnose our cases earlier, diet, abstinence from alcohol and other toxic agents would be all that would be necessary. Lately choline has been used more or less experimentally in cases of cirrhosis of the liver. During the last year I have used it perhaps in 15 cases. Some of these patients went along and died promptly, not because of the choline but in spite of it. Other patients have remained about the same and some have improved. However, these patients have received a diet such as Dr. Greene has prescribed and the necessary vitamins and iron when iron deficiency was apparent, so that it seems hardly likely to me from these cases and from reading the reports of a few others in which choline has been used that we can expect very much from this form of treatment. The use of amino acids in bringing up the plasma proteins has to me been very discouraging. I have used it both parenterally and by mouth in pretty large doses and do not believe that it has caused any elevation of the plasma proteins in the cases in which I have used it. The remarkable effects that I have noticed in cases of severe plasma protein deficiencies associated with ascites have been the result of the infusion of plasma itself. This, of course, is an expensive form of treatment, but if one gives from 250 to 500 cc. every two or three days until 3,000 cc. has been given the most remarkable result appears in many cases. Plasma proteins become elevated and a great diuresis results. The ascites may not reform for quite a long time before more plasma is necessary. To date, however, it appears to me that the most important advance in treatment is the dietetic one associated with the use of vitamins and iron when necessary. However, there still remains the problem of getting these patients to eat. Many of them, of course, do not have a particularly good appetite. That brings up the question of preparing food concentrates. I have been employing various soybean preparations and, strangely enough, although I don't like them myself, many patients do, and we have been able to give them a much higher carbohydrate-protein diet with the use of the soybean preparations than in any other way.

Dr. Carl H. Greene, New York: The discussion has emphasized one point that I did not have time to make—the change in the qualitative nature of the proteins. I think the change in the character of the proteins is the factor responsible for the clinical value of such qualitative tests as the Takata-Ara and more recently the Hanger flocculation test. The latter is of especial diagnostic value in early diagnosis. I did not take up the question of bile salts because they are of no therapeutic importance in portal cirrhosis and I doubt if they have very much in biliary cirrhosis. My own experience has convinced me that the damaged liver does not respond well to bile salts. It cannot pick them up and it does not secrete them too well. I don't think they are safe in whipping up a damaged liver. Dr. Yater mentioned the use of amino acids intravenously. That is a valuable procedure in a selected series of cases, but when one can get the patient to take it by mouth I think it is preferable to give the extra protein by mouth rather than intravenously. I am glad Dr. Yater's experience with plasma has been similar to my own. He brought out the one determining factor in my work and that was the question of expense. For many of these patients plasma is so expensive that it is prohibitive. Under these conditions if one is fortunate the patient's own ascitic fluid can be used as a much cheaper substitute.

THE GASTROINTESTINAL TRACT AND THE LIVER

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The anatomic, physiologic and pathologic relations between the gastrointestinal tract and the liver are discussed frequently, but many problems arising from these relations remain unexplored. It is my purpose to present some of these problems with the view of emphasizing their probable importance rather than supplying an answer to them.

The liver can rightly be considered as one of the organs of digestion because it produces a secretion which is passed into the intestine and which is important in the maintenance of normal digestion. However, the liver is of much more significance in relation to the digestive tract than being merely one of the organs producing a digestive secretion. It is in addition the organ through which most of the products of digestion pass before reaching other tissues of the body. In this capacity it can be considered as a filter of the blood that has passed through the organs that have to do with the digestion and absorption of a large percentage of the food substances that enter the body.

The pathway between the gastrointestinal tract and the liver is the portal circulation. All the blood from the gastrointestinal tract, spleen and pancreas, except the small amount that drains through collateral channels, passes through the liver. The portal circulation therefore is of considerable importance, not only in a consideration of coordination of functions of the gastrointestinal tract and the liver, but also in relation to the development of pathologic conditions in the two organs.

SPECIFIC CHARACTERISTICS OF THE PORTAL SYSTEM

The portal system has several characteristics, some of which are particularly pertinent to hepatic activity. The portal vein drains one of the most vascular regions in the body. The amount of blood that reaches the liver through the venous component of the hepatic circulation may be relatively very large. Since the blood in the portal vein must pass through the capillaries and sinusoids of the liver before reaching the systemic venous system, the pressure in the portal vein is normally higher than it otherwise would be. The vasomotor control of the blood flowing through the portal vein is located in the organs which are drained into the portal system. Thus the major source of blood supply to the liver is not controlled within the organ, although the total outflow from the liver may be temporarily restricted by a mechanism located in the small hepatic veins.[1]

From the Division of Experimental Medicine, Mayo Foundation.

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THE LIVER AS A FILTER OF THE BLOOD FROM THE GASTROINTESTINAL TRACT

Beginning in fetal life, many of the substances that reach the other tissues of the body must first pass through the liver. Evidence indicating the importance of this anatomic fact in relation to hepatic activity and the development of pathologic conditions in the organ is much more meager than the speculations regarding it. Most of the theories in this regard have dealt with the detoxifying functions of the organ. Data proving that the liver has an enhanced physiologic activity with regard to specific substances owing to their higher content in the portal blood as compared with their content in the systemic blood are few. It has been shown that some substances, as strychnine,[2] are readily destroyed in the liver, that transformation of dextrose into glycogen appears to be greater when the content of the former in the portal blood is high,[3] that relatively large amounts of colloidal substances are removed from the portal blood by the stellate cells in a single passage through the organ [4] and that dyes can be injected into the portal vein in amounts which will stain the liver but not cause a discernible coloration in other tissues of the body.[5] Such evidence would indicate that the liver does serve as a filter for the portal blood but the full import of hepatic activity in this respect requires further investigation. The results of investigations on this problem may be of significance in the evaluation of those liver function tests in which the test substance is administered orally.

AMOUNT OF PORTAL BLOOD FLOW

The liver possesses two sources of blood supply, arterial and venous. Questions concerning the circulation of the liver have dealt, not only with the total amount of blood flow to the organ, but also with the relative amount from each source and whether or not the blood from the separate sources served different functions. Answers to these questions have been obtained in part. Measurements of the amount of blood flowing to and from the liver indicate that the total amount of blood flow to the organ is relatively large and varies within wide limits; that the relative amount of the total flow reaching the organ through either the arterial or venous component likewise varies greatly although the flow through the portal vein is always much greater than through the hepatic artery; that often there is a reciprocal response between the flow in the portal vein and hepatic artery; [6] that under certain conditions the flow can be increased or decreased simultaneously in each and under other conditions increased separately in each; [7] that in general, substances that stimulate the liver, as bile salts, increase the blood flow mainly in the artery.[8]

CHANGES IN PORTAL BLOOD FLOW

Under certain physiologic conditions the flow of blood in the portal vein can be greatly increased. The best examples of physiologic states that are accompanied by increase in portal blood flow are digestion and exercise. The ingestion of a meal is followed by an increase in flow of blood throughout the body and the blood flow in the portal vein is also increased greatly.[9] Likewise there is an increased flow of blood through the portal vein as well as to the muscles in muscular exercise.[10] It is presumed that increased hepatic activity is associated with the greater flow of blood. It is assumed that both digestion and exercise produce an increase of functional stress on the liver. The giving of functional tests under the stress of digestion or exercise might supply data that would be of physiologic as well as clinical value.

CHARACTER OF FLOW OF BLOOD IN THE PORTAL VEIN

The character of flow of blood in the portal vein appears to be important. Considerable evidence has accumulated which indicates that the flow in the portal vein is streamlined. The results of experiments in which india ink, dyes, emulsions of oil and other substances have been injected into various tributaries of the portal vein and their site of localization in the liver has been determined, as well as direct observation of the flow in the vein by transillumination, demonstrate that the blood in the portal vein originating from various sources is not completely mixed. There is a selective distribution of portal blood in the liver. The blood from the upper part of the gastrointestinal tract and spleen goes mainly to the left portion of the organ, while the rest of the portal blood has a greater distribution and goes to the right side.[11]

The importance of this selective distribution of portal blood from different sources in the liver is not known and the problems involved are mainly unexplored, but some theoretical considerations may indicate its possible significance. Food products that are absorbed from the upper loops of the intestine go mainly to the left portion of the liver while the absorption products from the lower portion of the intestine pass in a larger amount through the right side. If food substances are given in form and amount so that absorption occurs in a localized length of intestine, only a relatively small portion of the liver will receive the portal blood that contains the high concentration of absorbed substances. It would appear that, if the whole liver is to function as a filter for the products of digestion, the ingested meal should be of such an amount and contain such types of food as would insure absorption from the entire length of intestine. It is conceivable that reactions to certain specific food substances may be due to the fact that such substances are absorbed so quickly from the upper portion of the intestine that the localized region of the liver through which they pass may be unable to prevent their reaching the systemic circulation in a sufficient concentration to cause an effect. The decreased toxicity of certain substances when given with food may be in part due to the specific distribution of portal blood in the liver.

While the previous statements have been concerned with the absorption of food, they would appear to be

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pertinent also to the absorption of those substances used in hepatic function tests that are administered orally. It is worthy of question whether such substances, administered in a fasting state, pass through more than a limited amount of hepatic tissue before reaching the general circulation. The difference, as far as circulating through the liver is concerned, between substances administered orally and intravenously may not be great. Comparative tests, in which the orally administered test substance would be given in the fasting state and with an inert meal which would insure absorption from the entire length of small intestine, might give different results.

Theories concerning the action of a substance as predicated on its effect in passing through the liver before reaching the systemic circulation should take the specific distribution of blood from the different organs draining into the portal system into consideration. One example can be given. Higgins and I [12] injected gentian violet into the vein which drains the major portion of the pancreas in the rat and found that the left lobes of liver were stained by the dye while the right lobes were unstained. Evidently the right half of the liver receives insulin in a concentration no greater than the other tissues of the body.

The production of a localized lesion in the liver by a toxic substance gaining entrance to the portal circulation through the gastrointestinal tract has been difficult but can be easily accomplished with the spleen as the port of entry. Bollman and I [13] injected carbon tetrachloride repeatedly into the spleen and produced an atrophic form of cirrhosis in the left lobes of the liver which was associated with a compensatory hypertrophy of the other lobes of the organ.

EFFECT ON THE LIVER OF LOSS OF PORTAL CIRCULATION

The importance of the portal circulation to the liver is emphasized by the changes produced in the organ by the loss of the blood reaching it through the venous component of its circulation. When the blood in the portal vein is diverted from its normal course directly into the vena cava, the liver atrophies to approximately half its normal size or less and certain definite changes in its gross and microscopic appearance occur which are almost characteristic.[14] The effects on the liver produced by loss of portal blood supply are due not only to the great decrease in total blood supply but also to the fact that certain localized regions of the hepatic lobule receive little or no blood from the hepatic artery.[15] The capacity of the liver for restoration is almost completely abolished with the loss of blood from the venous component.[16] On the other hand, regeneration of hepatic tissue after injury appears to begin in the islands of seemingly normal hepatic cells that are supplied mainly or entirely by arterial blood while the cells in the regions supplied only by portal blood may be too badly injured to regenerate hepatic tissues.[17] Thus the intrahepatic portal pathways are gradually obliterated because the regions of hepatic tissue which they supply are not regenerated. This process not only decreases the amount of regeneration but also diverts portal blood into collateral channels. Since the functions of the portal blood and arterial blood to the liver are somewhat different, comparable tests of liver function in the condition of cirrhosis in which the test substance is administered orally and intravenously might furnish different results.

EFFECT OF DISTENTION OF INTESTINE ON PORTAL BLOOD FLOW

Alterations in the flow of blood in the portal vein depend on changes in the amount of blood that passes through the organs that drain into the portal system. Many conditions may affect the blood flow from one or more of these organs. One illustration will be given. Herrick and I [18] studied the effect of acute distention of the intestine with different pressures on portal blood flow and portal pressure. Our purpose in making the investigation was to determine if there was a basis for the possibility that distention of the intestine might affect hepatic activity by producing alterations in the portal circulation. Our results will be given briefly without reference to the controversial phases of the subject. We found that the effect of distention of the intestine on the flow of blood in the portal vein was variable. Usually the flow decreased progressively with increases in intraintestinal pressures but occasionally the portal flow would increase slightly or remain unchanged. Pressure in the portal vein always increased and, when the intestine was greatly distended, almost equaled the intraintestinal pressure. Evidently distention of the intestine may produce alteration in the portal circulation to such an extent that hepatic activity could be affected.

EFFECT OF OBSTRUCTION OF BILIARY OUTFLOW ON INTESTINAL ACTIVITY

Alteration in the liver, either physiologic or pathologic, may affect the normal function of the intestine. This statement is especially pertinent to the condition of obstruction of the common bile duct. Obstruction of the biliary outflow and the retention of the constituents of the bile in the liver and other tissues throughout the body may affect the functions of the intestinal tract owing to (1) lack of bile in the intestine or (2) effect of retained constituents of bile on (*a*) intestinal secretion and (*b*) motor mechanism.

Observations on intestinal activity in the presence of jaundice are meager. Canonico and I [19] made an experimental study of intestinal activity before and after ligation of the common bile duct, using methods which permitted observation and recording of activity of loops of jejunum and ileum under nearly normal conditions. We found that biliary obstruction was followed by a definite decrease of activity in the loops of intestine under observation during the first two weeks after operation. Intestinal activity subsequently increased but never equaled the normal amount in the jaundiced animal. A comparison of the activity of the intestine before and after obstruction of the common bile duct showed that, although the decrease occurred in both the fasting and digesting states, it was more noticeable in the latter. Some suggestive evidence was obtained indicating that the biliary constituents retained in the blood, particularly the bile salts, may be of importance in causing the decreased intestinal activity noted.

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LIVER FUNCTION TESTS

A GENERAL EVALUATION OF LIVER FUNCTION TESTS, AND AN APPRAISAL OF THE COMPARATIVE SENSITIVITY AND RELIABILITY OF THE NEWER TESTS, WITH PARTICULAR EMPHASIS ON THE CEPHALIN-CHOLESTEROL FLOCCULATION TEST, THE INTRAVENOUS HIPPURIC ACID TEST AND AN IMPROVED BROMSULPHALEIN TEST WITH A NEW NORMAL STANDARD

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This discussion deals, first, with a general evaluation of liver function tests and with the importance of adequate and carefully conducted normal control studies. In the second place, the comparative sensitivity and reliability of the newer tests, in relation to each other and to the older tests, as evaluated in a recent publication of ours,[1] are reviewed and summarized. Finally, an improved bromsulphalein method has been developed, using 5 mg. of the dye per kilogram and employing a new time interval as the normal standard for complete disappearance of the dye from the blood stream.

GENERAL EVALUATION OF LIVER FUNCTION TESTS

Liver function tests offer valuable aid in the evaluation of hepatic cell function. However, these tests should be regarded only as an aid to clinical and other laboratory findings in the diagnosis of the exact pathologic conditions. Liver function tests indicate the existing functional state of the hepatic cells but they do not reveal the cause of the impaired function. They do not indicate whether impaired function is due to a toxin circulating in the blood stream, an acute or chronic infection, faulty diet, compression of liver cells by scar tissue or metastatic carcinoma within the liver or to any one of several other causes. Nor do these tests indicate whether the underlying cause is an acute condition or a more serious, chronic, progressive type of hepatic disease. However, if one knows from clinical and other laboratory or x-ray studies the general nature of the pathologic condition, then the results of the liver function tests are of unusual value. They assume real importance in preoperative and postoperative treatment and in evaluating the degree of impairment, the effectiveness of medical treatment, and the prognosis.

From the practical point of view of the clinician, a basis for liver function tests is being developed on which they do measure, either directly or indirectly, the capacity of the liver to function adequately under various circumstances. To achieve this objective the most urgent need is for normal control studies to demonstrate more accurately the extent of normal variations and to denote more exactly the line of demarcation between normal and abnormal hepatic function. That the newer liver function tests do measure something of practical importance is evidenced by the close parallelism between changes in the results of these tests and changes in the clinical picture. It has been demonstrated that these tests have both diagnostic and prognostic value.

Probably the most convincing, specific evidence that liver function tests do measure the impairment of liver function is found in a study of "catarrhal jaundice," or acute toxic degenerative hepatitis. In this condition, in which the essential pathologic change consists in a destruction of many liver cells, followed by a gradual regeneration of normal liver cells, the liver function tests show a maximum deviation from normal relatively early in the course of the disease. As clinical evidence of hepatic repair develops, there is a continued and close parallelism in the improvement of the hepatic function tests.

In employing different liver function tests in identical cases one is impressed by the fact that there is no constant correlation of the results obtained with different tests. For example, in 1 case tests A and B may both show impairment of liver function, in a second case test A may show impairment and test B no evidence of it and in a third case only test B may show impairment. This common observation can best be explained, Mann [2] has emphasized, by the hypothesis that the various functions of the liver are not injured equally under different conditions. There is a dissociation of impairment of different liver functions and a corresponding dissociation of the results of liver function tests.

Therefore, the wisdom of conducting several different types of hepatic function tests is obvious, if one expects to demonstrate evidence of impaired liver function in the greatest percentage of patients with liver damage.

LITERATURE AND HEPATIC FUNCTION TEST METHODS

In a recent and much more comprehensive work [1] dealing with this same general subject, we reported the results of a comparative statistical study, conducted to determine the sensitivity and reliability of Hanger's cephalin-cholesterol flocculation test,[3] Quick's intravenous hippuric acid test,[4] a modification of Macdonald's 2 mg. per kilogram serial bromsulphalein method [5] and Gray's colloidal gold test [6] in relation to one another and to the two older tests, viz. the oral hippuric acid test [7] and the original Rosenthal bromsulphalein method.[8] The exact method used in the conduct of each test was outlined. The previous literature was reviewed in some detail.[1]

Normal control studies were conducted on 40 normal young adults [1] varying between 25 and 35 years of age. Normal standards for each test were determined which would afford the maximum sensitivity compatible with reliability for each test.

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Read before the joint meeting of the Section on Pathology and Physiology and the Section on Gastro-Enterology and Proctology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

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4. Quick, Armand J.; Ottenstein, Harold N., and Weltchek, Herbert: Synthesis of Hippuric Acid in Man Following Intravenous Injection of Sodium Benzoate, Proc. Soc. Exper. Biol. & Med. **38:** 77-78 (Feb.) 1938.

5. Macdonald, Dean: Some Observations on the Disappearance of Bromsulphalein Dye from the Blood: Its Relation to Liver Function, Canad. M. A. J. **39:** 556-560 (Dec.) 1938.

6. Gray, Seymour J.: The Colloidal Gold Reaction of Blood Serum in Diseases of the Liver, Arch. Int. Med. **65:** 524-544 (March) 1940.

7. Quick, Armand J.: The Synthesis of Hippuric Acid: A New Test of Liver Function, Am. J. M. Sc. **185:** 630-635 (May) 1933.

8. Rosenthal, Sanford M., and White, Edwin C.: Clinical Application of the Bromsulphalein Test for Hepatic Function, J. A. M. A. **84:** 1112-1114 (April 11) 1925.

In the conduct of the cephalin-cholesterol flocculation test on normal individuals it was learned that the test is reliable only if (1) unripened cephalin is used, as advised in Hanger's original publication,[8] and (2) if the 1 plus tests are regarded as within normal limits, and positive diagnostic importance is attached only to 2 plus, 3 plus and 4 plus tests. (Ripened cephalin studies on normal controls yielded numerous false positive 2 plus and 3 plus results, whereas unripened cephalin yielded only 12.5 per cent of false positive results, and only 1 plus results with the normal controls.)

Normal control studies with Quick's intravenous hippuric acid method completely corroborated Quick's statement that any urinary output of less than 0.70 Gm. of benzoic acid as hippuric acid in the one hour urine specimen indicates some degree of impairment of hepatic function.

The normal control studies with a modified serial 2 mg. per kilogram bromsulphalein method (obtaining blood specimens every five minutes for thirty minutes after injection of the dye) revealed the fact that twenty minutes is the normal time for complete disappearance of the dye from the blood stream when the aforementioned dose is used and not thirty minutes, as previously assumed. Therefore, if one wishes to withdraw only a single blood specimen after injecting a 2 mg. per kilogram dose of the dye, instead of using the serial method, one should withdraw the one blood specimen in exactly twenty minutes rather than in thirty minutes.

The results of the normal control studies with the colloidal gold test will not be referred to here, since this test was found not to be adapted to routine laboratory use.

COMPARATIVE SENSITIVITY AND RELIABILITY OF THE NEWER LIVER FUNCTION TESTS

In the comparative study of the sensitivity of the four newer hepatic function tests referred to, in relation to the two older tests, viz. the oral hippuric acid test and the Rosenthal bromsulphalein method (2 mg. dose of the dye administered and a single blood specimen withdrawn thirty minutes later), the following results were obtained in a direct comparison of each test with every other test, when conducted on an identical group of subjects.[1]

The intravenous hippuric acid test yielded 85 per cent more positive tests than the oral hippuric acid test. This much greater sensitivity of the intravenous test is due to reasons previously specified.[1] The serial bromsulphalein method, using the 2 mg. per kilogram dose of the dye and twenty minutes as the normal clearance time for the dye, yielded 100 per cent more positive tests than the thirty minute Rosenthal bromsulphalein method. The cephalin test yielded exactly the same number of positive tests as the intravenous hippuric acid test but 33 per cent more positive tests than the aforementioned serial bromsulphalein test.

A study of the relative sensitivity of these various tests in various pathologic groups of cases indicated that all four of the newer tests (including the colloidal gold test, which is not satisfactory for other reasons) are appreciably more sensitive than the two older tests. Of special interest was the observation that in a group of 67 patients with gallstones, studied before operation, 53 per cent yielded a positive intravenous hippuric acid test, 50 per cent a positive cephalin test and 42 per cent yielded a positive, serial, twenty minute, 2 mg., bromsulphalein test, whereas only 15 per cent yielded a positive Rosenthal bromsulphalein test. This type of information is of great practical value in selecting cases of cholelithiasis needing special preoperative preparation.

The oral hippuric acid test, although much less sensitive than the three newer tests, has one important advantage in a particular group of cases, first, because it is less sensitive and a greater degree of liver impairment is necessary to yield a positive test, and, second, because the extensive use of this test over some period of time has led to its well established evaluation. This test has a proved value in determining the operability of patients with known liver damage. Snell,[9] White [10] and we agree that if there is less than 50 per cent of the normal 3 Gm. of hippuric acid excreted in the four hour urine collection, viz., less than 1.5 Gm., this finding indicates that such a patient presents a very poor operative risk.

ADVANTAGES AND LIMITATIONS OF EACH TEST

The various advantages and limitations of each of the four newer tests and the two older tests have been outlined.[1] These deductions will not be repeated here.

AN IMPROVED BROMSULPHALEIN TEST

In the recent literature advocating the 5 mg. per kilogram dose for the bromsulphalein test, one finds a wide variation in the normal standard adopted by different workers. This situation is apparently due to taking inadequate precautions in establishing the exact range of normal variations. To avoid this pitfall two precautions would seem necessary: First, in the study of normal individuals to establish the correct normal standard, it seems absolutely essential to conduct a serial type of examination after injection of the dye, withdrawing a blood specimen for dye estimation every five minutes until after the dye has completely disappeared from the blood. Only in this way can the normal disappearance time be accurately determined and variations in the normal disappearance time of the dye correctly defined. In the second place, it is obviously important to study an adequate number of normal individuals if the resulting normal standard is to represent the full range of normal variations. Reported studies of 8, 10 or 12 normal individuals represent an inadequate number of controls.

A New and Improved Normal Standard for the 5 Mg. per Kilogram Bromsulphalein Test.—In table 1 are presented the results of a study of thirty normal control individuals studied by the serial 5 mg. per kilogram bromsulphalein method. In this group of healthy persons ranging from 25 to 35 years, with no history of catarrhal jaundice or of any type of chronic gastrointestinal symptoms, who had received 5 mg. of bromsulphalein per kilogram, the dye had completely disappeared from the blood stream in 73 per cent of these normal controls in thirty minutes, in 86 per cent in thirty-five minutes, in 96 per cent in forty minutes and in 100 per cent of these normal individuals in forty-five minutes. The forty-five minute period has been adopted, therefore, as the normal standard for complete disappearance of the dye after injection of 5 mg. of bromsulphalein per kilogram.

9. Snell, Albert M., and Plunkett, John E.: The Hippuric Acid Test for Hepatic Function: Its Relation to Other Tests in General Use, Am. J. Digest. Dis. & Nutrition **2**: 716-721 (Feb.) 1936.

10. White, Franklin W.; Deutsch, Emmanuel, and Maddock, Stephen: The Comparative Value of Serial Hippuric Acid Excretion, Total Cholesterol, Cholesterol Ester and Phospho Lipid Tests in Diseases of the Liver, Am. J. Digest. Dis. **6**: 603-610 (Nov.) 1939.

11. Footnote deleted on proof.

It is important to have a normal standard which yields no false positive tests with healthy young adults. At the same time it is not necessary to allow a longer period than the one which just fails to give any false positive results in the entire normal control group. In offering this new recommendation, that the result of this test be interpreted as normal or abnormal, depending on whether the dye has or has not completely disappeared from the blood in the forty-five minute specimen, the reliability of this time interval is enhanced when one realizes that the dye had completely disappeared from the blood in 86 per cent of the normal group in thirty-five minutes, and that the additional ten minutes is allowed to insure the diagnosis of normal liver function in the remaining small 14 per cent subgroup of normal persons. Sensitivity of any test is advantageous only as far as it is associated with reliability.

TABLE 1.—*Study of 30 Normal Young Persons with Serial Blood Estimations of Residual Dye to Determine Correct Normal Standard for 5 Mg. per Kilogram Bromsulphalein Test* *

(2 Mg. per Kilogram Bromsulphalein Test Also Done for Comparison †)

Normal Controls, No.	5 Mg. per Kilogram BSP Test-Minutes									2 Mg. per Kilogram BSP Test-Minutes					
	5	10	15	20	25	30	35	40	45	5	10	15	20	25	30
1.....	60	30	10	5	Trace	Trace	0	0	0	45	20	Trace	0	0	0
2.....	40	20	5	Trace	0	0	0	0	0	25	10	5	0	0	0
3.....	50	20	10	5	Trace	0	0	0	0	30	5	0	0	0	0
4.....	50	18	7	5	Trace	0	0	0	0	55	25	10	0	0	0
5.....	80	30	15	10	6	4	2	0	0	45	20	0	0	0	0
6.....	60	25	15	5	0	0	0	0	0	30	10	0	0	0	0
7.....	60	30	5	Trace	0	0	0	0	0	35	7	Trace	0	0	0
8.....	40	17	6	4	0	0	0	0	0	60	20	5	0	0	0
9.....	35	15	5	Trace	0	0	0	0	0	25	5	0	0	0	0
10.....	35	20	10	5	Trace	0	0	0	0	30	5	0	0	0	0
11.....	30	20	8	Trace	Trace	0	0	0	0	27	5	0	0	0	0
12.....	60	30	20	10	Trace	0	0	0	0	27	10	0	0	0	0
13.....	35	20	10	5	Trace	0	0	0	0	30	5	Trace	0	0	0
14.....	50	10	5	Trace	Trace	0	0	0	0	30	7	0	0	0	0
15.....	35	25	15	5	Trace	0	0	0	0	30	7	0	0	0	0
16.....	60	24	11	4	Trace	Trace	0	0	0	45	15	5	0	0	0
17.....	50	20	10	Trace	Trace	0	0	0	0	40	12	5	0	0	0
18.....	50	20	6	4	Trace	0	0	0	0	30	5	0	0	0	0
19.....	80	60	40	8	Trace	0	0	0	0	25	5	0	0	0	0
20.....	70	25	10	Trace	0	0	0	0	0	40	15	Trace	0	0	0
21.....	25	8	Trace	Trace	0	0	0	0	0	27	7	0	0	0	0
22.....	95	50	20	17	16	10	5	2	0	25	5	0	0	0	0
23.....	45	15	5	Trace	0	0	0	0	0	25	10	0	0	0	0
24.....	30	20	10	Trace	Trace	Trace	0	0	0	35	10	0	0	0	0
25.....	50	40	20	10	Trace	Trace	0	0	0	45	15	5	0	0	0
26.....	..	..	20	12	6	2	Trace	0	0						
27.....	..	..	10	6	4	2	Trace	0	0						
28.....	..	..	14	8	Trace	0	0	0	0						
29.....	..	..	10	4	0	0	0	0	0						
30.....	..	..	8	2	Trace	0	0	0	0						

* With the 5 mg. per kilogram dose of dye it is noted that the dye has disappeared from the blood in every normal person in forty-five minutes, whereas the normal disappearance time for the 2 mg. per kilogram dose was twenty minutes.

† All of these 30 normal persons also yielded a negative cephalin test, according to the normal standard recently established.

As already noted, in the rather scant recent literature dealing with the use of the 5 mg. per kilogram dose of bromsulphalein one finds a wide variation in the standard that has been adopted as normal by different workers.

Several have advised obtaining a single blood specimen in thirty minutes and specifying 6, 8 or 10 per cent retention as the maximum retention for a normal test. For example, Israel and Reinhold [12] regarded any retention of more than 6 per cent in thirty minutes as abnormal, whereas Rosenberg and Soskin [13] accepted a retention of dye varying from 0 to 10 per cent in thirty minutes as within normal limits. Any of these standards which attempt to fix a particular percentage of dye retention as the upper limit of normal are open to one important criticism. For example, one person may exhibit 10 per cent retention of the dye in thirty minutes, and the dye may have completely disappeared from the blood in forty-five minutes. Another person may exhibit the same 10 per cent retention of dye in thirty minutes, but 4 or 5 per cent may still be present in forty-five minutes. This prolonged delay in the disappearance of the last small percentage of dye from the blood is quite characteristic of impaired liver function and will be noted in numerous cases if the serial bromsulphalein method is used. This fact has not been appreciated generally, because the serial method has not been employed.

On the other hand, those workers who have used a normal standard based on the complete disappearance of dye from the blood have used either thirty minutes or sixty minutes as the normal disappearance time of the dye. This wide variation again in normal standards is due apparently, as already noted, either to (1) a failure to use the serial method in determining the normal standard, (2) to studying an insufficient number of normal controls or (3) to not using sufficient care in selecting the cases that are used for normal control studies.

Although reliable, the allowance of sixty minutes for the normal clearance time of a 5 mg. per kilogram dose of the dye detracts from the legitimate sensitivity of the test, since the normal control studies by the serial method shown in table 1 indicate that this time standard is unnecessarily generous and would fail, therefore, to detect an appreciable number of cases with slight but definite impairment of liver function. On the other hand, Helm and Machella [14] have recently advocated

12. Israel, H. L., and Reinhold, J. G.: Detection of Cirrhosis and Other Diseases of the Liver by Laboratory Tests, J. Lab. & Clin. Med. **23**: 588-596 (March) 1938.

13. Rosenberg, D. H., and Soskin, Samuel: Azorubin S Test of Liver Function: Evaluation with Comparative Study of Bromsulphalein and Hippuric Acid Tests, Ann. Int. Med. **13**: 1644 (March) 1940.

14. Helm, John D., and Machella, Thomas E.: The Significance of Dosage and Time Factors on the Value of the Bromsulphalein Test for Liver Function, Am. J. Digest. Dis. **9**: 141-143 (April) 1942.

thirty minutes as the proper normal disappearance time for the 5 mg. per kilogram dose of dye. Our normal control studies by the serial method indicate that thirty minutes is too short a time and would render the test too sensitive. This time interval would yield, therefore, false positive tests. In 27 per cent of our normal control subjects the dye had not cleared from the blood in thirty minutes, although it had disappeared at this time in the other 73 per cent. The probable explanation as sensitive as either the cephalin test or the intravenous hippuric acid test and at the same time a test which is just as reliable.

Serial Specimen, Single Specimen or Two Specimen 5 Mg. Bromsulphalein Method (forty-five minute dye disappearance time).—From the standpoint of economy of time and effort a single forty-five minute specimen is satisfactory, since this correct normal standard has been determined by the serial method. Such a

TABLE 2.—*Sensitivity of 5 Mg. per Kilogram Serial Bromsulphalein Test as Compared with That of Cephalin-Cholesterol Flocculation Test and That of 2 Mg. per Kilogram Serial Bromsulphalein Test* *

Case No.	Cephalin Test	2 Mg. Bromsulphalein Test-Minutes							5 Mg. Bromsulphalein Test-Minutes							Diagnosis
		5	10	15	20	25	30	35	15	20	25	30	35	40	45	
1	2+	40	35	30	20	20	15	10	30	20	16	14	14	14	14	Metastatic carcinoma
2	3+				N.D.†				25	25	20	15	15	15	10	Portal cirrhosis ‡
3	0	25	Trace	0	0	0	0	0	24	22	20	18	14	4	0	Enlarged liver #
4	3+				N.D.				38	32	28	22	20	18	16	Enlarged liver #
5	1+	25	10	Trace	0	0	0	0	25	18	15	12	10	8	6	Portal cirrhosis
6	4+	70	60	50	45	45	35	30	55	48	42	38	36	35	33	Portal cirrhosis
7	0	45	15	Trace	0	0	0	0	20	14	10	8	6	4	2	Gallstones
8	4+	35	25	15	5	Trace	0	0	24	18	14	10	8	6	4	Portal cirrhosis
9	2+				N.D.				36	28	24	20	18	16	14	Metastatic carcinoma
10	4+	40	15	Trace	0	0	0	0	10	8	6	4	3	2	Trace	Gallstones
11	1+	55	30	20	Trace	0	0	0	12	5	0	0	0	0	0	Enlarged liver
12	2+	45	10	Trace	0	0	0	0	10	5	Trace	0	0	0	0	Cholecystitis
13	4+				N.D.				2	Trace	0	0	0	0	0	Gallstones
14	0	45	15	5	0	0	0	0	15	10	5	Trace	0	0	0	Cholecystitis
15	2+	32	12	5	0	0	0	0	2	Trace	0	0	0	0	0	Enlarged liver
16	N.D.	30	7	2	0	0	0	0	20	16	13	12	12	11	10	Metastatic carcinoma
17	N.D.	15	10	Trace	0	0	0	0	11	6	3	1	Trace	Trace	0	Gallstones
18	0	27	15	5	0	0	0	0	30	16	10	8	6	4	3	Gallstones
19	0				N.D.				8	4	3	2	1	Trace	0	Enlarged liver
20	0	35	10	2	0	0	0	0	8	4	3	2	Trace	0	0	Gallstones
21	0	25	5	Trace	0	0	0	0	18	10	6	4	2	1	Trace	Alcoholism
22	4+				N.D.				8	4	3	2	1	Trace	Trace	Enlarged liver
23	0	15	5	0	0	0	0	0	Trace	0	0	0	0	0	0	Gallstones
24	0	15	5	0	0	0	0	0	10	2	0	0	0	0	0	Alcoholism
25	4+	40	17	10	5	Trace	0	0	30	20	15	10	5	5	0	Portal cirrhosis
26	0	40	20	5	0	0	0	0	20	12	6	4	2	Trace	0	Portal cirrhosis
27	1+				N.D.				16	7	2	Trace	0	0	0	Enlarged liver
28	0	35	10	Trace	0	0	0	0	16	6	4	4	3	2	1	Portal cirrhosis
29	0	25	16	5	0	0	0	0	40	24	16	12	10	8	4	Metastatic carcinoma
30	4+	40	12	5	0	0	0	0	13	5	3	1	Trace	0	0	Gallstones
31	0	15	5	0	0	0	0	0	20	15	5	Trace	0	0	0	Alcoholism
32	1+	35	15	Trace	0	0	0	0	20	10	8	7	5	4	1	Enlarged liver
33	3+	27	10	2	Trace	0	0	0	12	8	2	1	Trace	0	0	Cholecystitis
34	4+	40	35	30	27	25	20	17	40	30	30	30	25	25	20	Portal cirrhosis
35	3+	30	10	0	0	0	0	0	6	4	2	Trace	0	0	0	Enlarged liver
36	2+				N.D.				8	5	4	2	1	Trace	0	Alcoholism
37	0	50	35	10	5	Trace	0	0	28	15	8	3	Trace	0	0	Alcoholism
38	0	27	8	0	0	0	0	0	16	12	8	5	2	Trace	0	Alcoholism
39	0				N.D.				16	12	10	8	6	5	4	Gallstones
40	0	30	10	Trace	0	0	0	0	12	8	6	4	2	1	0	Cholecystitis
41	4+				N.D.				18	12	6	2	0	0	0	Cholecystitis
42	3+	35	10	0	0	0	0	0	10	Trace	0	0	0	0	0	Cholecystitis
43	0				N.D.				17	14	12	12	12	12	10	Metastatic carcinoma
44	4+				N.D.				32	28	24	20	14	12	10	Enlarged liver
45	4+				N.D.				13	8	6	2	1	Trace	Trace	Enlarged liver
46	0				N.D.				30	16	12	8	6	4	3	Enlarged liver

* 5 mg. dye test and cephalin test were conducted in 44 of the 46 cases listed in this table; 5 mg. dye test and 2 mg. dye test were conducted in 32 of the 46 cases listed.

† N.D. indicates that the test so specified was not conducted in this particular case.

‡ These cases of "portal cirrhosis" all presented some evidence of portal obstruction (e. g. ascites, superficial collateral circulation or other evidence).

These cases of "enlarged liver" all presented either an alcoholic history or evidence of chronic gall tract disease in addition to some degree of enlargement of liver.

why Helm and Machella found the blood free from dye in thirty minutes in all their normal controls was that they report studying only 12 normal persons.

In this study of an improved 5 mg. per kilogram bromsulphalein method, all estimations of the amount of retained dye in the blood have been conducted with a specially prepared 5 mg. colorimetric standard which measures any residual dye in terms of percentage of the amount of dye originally injected.

The forty-five minute interval advocated in this publication for normal disappearance of the dye from the blood with the 5 mg. per kilogram dose constitutes a new standard, which, as will be noted, provides a test single specimen affords the necessary information, provided it is taken exactly at the proper time. A compromise between the serial and single specimen method, which would constitute the most desirable method from a comprehensive point of view, would consist in obtaining a forty-five minute and sixty minute blood specimen, with separate venipunctures. This would avoid the need for giving intravenous saline solution to keep the needle open, when using the serial method and obtaining a number of blood specimens. At the same time, obtaining a sixty minute specimen, in addition to the forty-five minute specimen, would supply supplementary information regarding the degree of impaired

liver function in those cases presenting evidence of impairment in the forty-five minute specimen. Thus the further rate of excretion of the dye can be demonstrated in this group of cases.

Results Obtained with Improved Bromsulphalein Test (forty-five minute normal standard 5 mg. per kilogram dose).—In table 2 the results of the serial, 5 mg. per kilogram, forty-five minute bromsulphalein method are compared (1) in 44 cases with the results obtained with the cephalin test in this same group of cases, and (2) with the results of the serial, 2 mg. per kilogram, twenty minute bromsulphalein method with the 32 patients studied by these two serial dye methods. (In all, 46 patients were studied.)

Like the group of 307 cases previously studied,[1] this group of 46 cases also included not only cases in which clinically obvious liver disease was present but also a number of cases of cholelithiasis, in which the hepatic impairment, when present, is usually of lesser degree. It is important to include cases of only slight and moderate impairment, as well as more advanced cases, when attempting to demonstrate the sensitivity of any liver function test.

It is noted in table 3 that the 5 mg. bromsulphalein test yielded exactly the same number of positive tests as the cephalin test and therefore exhibited the same degree of sensitivity, provided the recommended forty-five minute disappearance time for the dye is regarded as a normal standard. It is also recalled that the intravenous hippuric acid test possesses approximately the same degree of sensitivity as the cephalin test. Therefore these three tests possess about the same sensitivity.

In comparing the sensitivity of the 2 mg. and 5 mg. bromsulphalein methods, using twenty minutes as the normal disappearance time of the dye for the 2 mg. method and forty-five minutes for the 5 mg. method, and utilizing the 32 cases in table 2, in which both dye methods were conducted, the following results were obtained. It is noted that the 2 mg. test was positive in a total of 8 cases and the 5 mg. test in a total of 13 cases. The 5 mg. test was therefore positive in 62 per cent more cases than the 2 mg. test, and the 5 mg. dose represents an appreciably more sensitive test than the 2 mg. dose.

The Influence of Variable Normal Standards in Producing Extreme Variations in Sensitivity of 5 Mg. Bromsulphalein Test.—When using various "normal" standards for the disappearance of the dye, as shown in table 3, extreme variations are exhibited in the sensitivity of the 5 mg. bromsulphalein method, as compared with the cephalin test. (The cephalin test was conducted with the constant, recently recommended, normal standard.[1]) For example, if thirty minutes is used as the normal standard for complete disappearance of dye from the blood, the 5 mg. per kilogram bromsulphalein test yields 76 per cent more positive tests than the cephalin test; if thirty-five minutes is used as the normal standard, the dye test is positive in 52 per cent more cases than the cephalin test; whereas if forty-five minutes, the most sensitive reliable normal standard for the 5 mg. dye test, is used the cephalin test and the 5 mg. per kilogram dye test yield exactly the same number of positive tests in the 44 cases (table 3). In other words, these two tests possess the same sensitivity provided both tests are conducted with a reliable technic which affords no false positive tests. If the serial dye test had been prolonged for sixty minutes, and sixty minutes had been regarded as the normal standard, it is obvious from tables 2 and 3 that the sensitivity of the 5 mg. dye test would have been appreciably reduced and that this test then would be much less sensitive than the cephalin test. In 54 per cent of the cases in table 2 showing a positive 5 mg. test with the forty-five minute standard, 4 per cent or less of the dye remained at forty-five minutes; and this small amount of dye would almost certainly have disappeared in sixty minutes in most cases, if the serial method had been continued to sixty minutes.

Another interesting fact apparent from table 3 is that, if some particular percentage of dye remaining in the blood at thirty minutes is used as the normal standard (instead of its complete disappearance), it makes a tremendous difference in the sensitivity of the dye test whether one uses as a normal standard an upper limit of 6 per cent of retained dye, as advised by Israel and

TABLE 3.—*Comparative Sensitivity of Cephalin-Cholesterol Flocculation Test and 5 Mg. per Kilogram Serial Bromsulphalein Test, Using Various Normal Bromsulphalein Standards in 44 Cases* *

Various Normal standards for BSP Test	No. of Cases Both Tests Positive	No. of Cases BSP Test Alone Positive	No. of Cases Cephalin Test Alone Positive	No. of Cases Both Tests Negative	Relative Sensitivity of Two Tests
1. 30 minutes = disappearance time †	17	20	4	3	76% more positive BSP tests
2. 35 minutes = disappearance time	15	17	6	6	52% more positive BSP tests
3. 40 minutes = disappearance time	13	15	8	8	23% more positive BSP tests
4. 45 minutes = disappearance time (normal standard recommended) ‡	11	10	10	13	Exactly equal sensitivity of BSP and cephalin tests
5. 60 minutes = disappearance time	..	..	..	..	Cephalin test would be appreciably more sensitive here #
6. Not more than 6% of BSP remaining in blood in 30 minutes	9	9	12	14	16% more positive cephalin tests
7. Not more than 10% of BSP remaining in 30 min.	7	2	14	21	133% more positive cephalin tests
8. Not more than 15% remaining in 30 minutes	5	1	16	22	250% more positive cephalin tests

* The statistics in this table are deduced from those in table 2. The use of the serial method has made possible the comparisons shown.

† If even a trace of dye remained at any of the various "normal" time standards referred to in this table, the test was interpreted as positive for that standard.

‡ That forty-five minutes is the correct normal standard for complete disappearance of the dye from the blood is indicated by the normal control studies listed in table 1.

The reason for this statement is discussed in the last section of this paper.

Reinhold, or an upper limit of 10 per cent, apparently the most commonly employed normal standard at the present time. If 6 per cent is regarded as the upper normal limit of dye retention, the cephalin test yields only 16 per cent more positive tests than the dye test, but if 10 per cent is regarded as the upper normal limit the cephalin test yields 133 per cent more positive tests than the 5 mg. bromsulphalein test. If 15 per cent of retained dye is regarded as the upper normal limit for thirty minutes (a standard which is also used) the contrast in sensitivity becomes even greater. With this 15 per cent upper normal limit of retained dye the cephalin test yields 250 per cent more positive tests than the 5 mg. bromsulphalein test.

The pronounced variations in the sensitivity of the 5 mg. dye test, occurring with the use of slightly different percentages of retained dye as the "normal" standard for the thirty minute specimen, constitute a second reason why it is undesirable to use any particular percentage of retained dye at thirty minutes as a normal standard. The first and still more important objection to using this type of a normal standard, in contrast to the complete disappearance of the dye at a later period, has been stated under the discussion of normal control studies.

POSTSCRIPT [15]

Since the paper was presented, certain additional observations and conclusions of considerable practical importance have been noted:

A. In further studies with different cephalin antigens an appreciable variation in their sensitivity has been noted. It has been observed that the sensitivity of freshly made unripened cephalin, if kept in a stoppered flask in the ice box, increases gradually on standing over a period of four or five months. For example, the cephalin-cholesterol flocculation test was conducted recently on the serums of 150 patients with clinical evidence suggesting liver impairment, parallel tests being run on the same serums with freshly prepared unripened cephalin and also with similarly prepared "unripened" cephalin which had remained in the ice box for about five months. The latter cephalin tended to yield more positive reactions, e. g. frequently a 3 plus reaction as opposed to a 1 plus reaction, or a 2 or 3 plus reaction as contrasted with a completely negative forty-eight hour reaction. In other words, the unripened cephalin did ripen somewhat on standing in the ice box.

When similar parallel tests were conducted on the serums of 20 normal young control subjects the freshly made cephalin yielded no positive tests, whereas with the cephalin which had stood in the ice box 2 of the 20 normal serums yielded a 1 plus test in the final forty-eight hour reading. None yielded a 2, 3 or 4 plus test.

In our initial observations with the cephalin-cholesterol flocculation test previously reported the cephalin used was cephalin which had not been ripened in sunlight but which had stood in the ice box about four months. The 40 normal serums tested with this cephalin yielded 12.5 per cent of 1 plus forty-eight hour results but no 2, 3 or 4 plus tests. In other words, the results were quite similar to those more recently obtained with cephalin which also had stood in the ice box an essentially similar period of time. With this type of cephalin 1 plus forty-eight hour results are not interpreted as being definitely positive.

Recent reports from other workers agree with our present impression that freshly made unripened cephalin is not sensitive enough to yield positive tests in a number of cases in which clinical or other evidence of impairment of liver cell function exists. The cephalin which has ripened in an ice box for four or five months is preferable. On the other hand, cephalin which had stood in the sunlight in an unstoppered bottle for a few weeks yielded numerous 2 and 3 plus false positive tests.

Recently several lots of a commercial preparation of cephalin (in the form of cephalin-cholesterol antigen ready for use), ripened in the sun by a special method and provided by the Difco Company of Detroit, have been tested. These lots yielded uniformly satisfactory results. The latter results ran almost exactly parallel to those obtained with the aforementioned cephalin which had stood in the ice box for five months. This commercial preparation was quite sensitive but yielded negative results throughout when tested against the serums of the 20 normal young subjects referred to except for a single serum (5 per cent), which yielded a negative result in twenty-four hours and only a 1 plus result in forty-eight hours. If this commercial antigen is used, at least a 2 plus result in forty-eight hours should be required, therefore, to indicate definite impairment of liver cell function.

The Difco Company has noted that the explanation of false positive results obtained on normal serums with certain sun ripened cephalin preparations consists in the fact that such antigens have not been ripened for a sufficiently long period of time.

B. The only objection to the 5 mg. per kilogram dose of bromsulphalein dye consists in the fact that some patients have a transient reaction to the injection of this larger dose of dye. Such a reaction develops in certain cases regardless of whether the injection of the dye is or is not followed by the injection of isotonic solution of sodium chloride and the employment of the serial method. The reaction may consist of transient headache, a feeling of faintness and in some cases a chill. These symptoms tend to occur from forty-five to sixty minutes after the injection of the dye. The headache may persist for several hours. No unfavorable or prolonged after-effect has been demonstrated. This type of reaction rarely occurs after employing the smaller dose of 2 mg. per kilogram of bromsulphalein.

C. In cases in which it is desired to determine mainly the presence or absence of a slight degree of impaired liver function, two or three of the most sensitive tests should be employed, e. g. the cephalin test, the 5 mg. per kilogram forty-five minute bromsulphalein test and the intravenous hippuric acid test.

In cases in which it is not only desired to determine the presence of impaired liver cell function but also to obtain from the tests as much information as possible about the degree of impairment, there is an important advantage in using several tests of varying sensitivity, e. g. the very sensitive cephalin test, the 2 mg. per kilogram twenty minute bromsulphalein test of intermediate sensitivity and the less sensitive oral hippuric acid test.

15. Added after paper was read.

THE SIGNIFICANCE OF MILD HYPERBILIRUBINEMIA IN GASTRO-INTESTINAL PATIENTS

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The routine use of serum bilirubin determinations on nonjaundiced patients discloses a group in which the serum bilirubin value is elevated beyond the usually accepted normal figure but in which there has been no evidence of preceding or subsequent jaundice. Such a group may be said to have latent jaundice.

The presence of an isolated elevated serum bilirubin value in a case in which the routine diagnostic survey discloses no other abnormality imposes certain diagnostic responsibilities on the clinician. Shall he ignore the hyperbilirubinemia? In terms of milligrams per hundred cubic centimeters of blood, at what level should one infer that a given value represents hyperbilirubinemia? Naturally the average patient, seeking relief from some real or fancied ailment, does not represent a normal individual, and a large group of similar patients, by virtue of the size of the group alone, cannot be considered a cross section of normal individuals. Nevertheless we believed that an analysis of a large group of patients who had submitted to a diagnostic study might afford some explanation for the presence of mild nonicteric hyperbilirubinemia. We are familiar with the fact that many observers, using the Thannhauser and Anderson[1] modification of the van den Bergh reaction, report normal values up to 1.5 or 2.0 mg. per hundred cubic centimeters of blood. Careful estimations of serum bilirubin by more accurate methods indicate that there is a large error inherent in the Thannhauser and Anderson method. The many reasons justifying this critical attitude toward the Thannhauser and Anderson method are well known and need not be reiterated here. Nevertheless some modification of the Thannhauser and Anderson method is in use in most institutions where the serum bilirubin is studied.

In an attempt to determine the basic pathologic condition behind a given case of hyperbilirubinemia, the clinician may approach the diagnostic problem by considering one of the following mechanisms:

1. Obvious obstructive jaundice of high degree due to calculus requires little comment. However, mild or latent icterus due to intermittent ball valve action of a calculus may require intensive study to verify the suspected causal factor. Cholecystography may supply the chief objective diagnostic criteria in this instance. In a small group of cases, wherein the cholecystogram is doubtful, biliary drainage may afford aid by the demonstration of calcium bilirubinate pigment and cholesterol crystals. In the older age group incipient malignant conditions of the biliary tract including lesions of the head of the pancreas and vaterian cancer must be ruled out. A progressive icterus usually but not invariably points toward a malignant process. Persistent occult blood in the stools may point toward malignancy of the pancreas or papillae of Vater. Varying degrees of hepatic dysfunction may occur in association with obstructive jaundice. Elevation of the serum phosphatase has been reported in obstructive jaundice, particularly when hepatic metastasis is suspected. We have derived comparatively little diagnostic help from the serum phosphatase in early icterus. An elevated serum lipase, in the absence of acute inflammatory pancreatic involvement, is almost pathognomonic of pancreatic malignancy.

2. Typical cases of hemolytic jaundice are rare. In most instances the critical data consist of a palpable spleen, varying degrees of anemia, reticulocytosis, spherocytosis and increased fragility of the red blood cells. Familial types of hemolytic anemia together with sickle cell anemia must be ruled out. One must not overlook the fact that occasionally many of the aforementioned diagnostic tests may be normal or present such a small variation from normality that the diagnosis may not be clear. Sternal marrow biopsy may prove of inestimable value in some instances. Certain stages of primary macrocytic anemia (primary pernicious anemia) may be present with hyperbilirubinemia.

3. Toxic hepatocellular mechanisms, including catarrhal jaundice, cholangitis and the various types of chronic infectious jaundice will need to be considered. Frequently the diagnosis of cases in this group is inferential. In most instances, however, the history, course of the disease and associated laboratory findings will indicate the type of involvement. The rapid onset of catarrhal jaundice in the younger age group, the rapidly changing and usually favorable clinical course, and a positive galactose tolerance test usually suffice to make the diagnosis. Occasionally an initial picture of catarrhal jaundice may merge into a mild latent icteric stage of varying duration. Acute yellow atrophy of the liver usually follows the exhibition of well known hepatotoxic drugs such as those containing the benzene ring, the arsphenamines, cinchophen and carbon tetrachloride. The recovery stage of acute yellow atrophy may be characterized by latent icterus. Subacute yellow atrophy in the absence of jaundice has been reported.

The term chronic cholangitis is a diagnostic pitfall and seems to be a convenient waste basket into which the busy clinician may cast cases of latent icterus which he cannot otherwise classify. Pathologically the distinction between mild catarrhal jaundice of the hepatocellular type and chronic cholangitis is difficult, and clinically the distinction may be impossible. The repeated recovery by bile drainage of plugs of mucus containing cellular débris and bacteria is said to be somewhat diagnostic of chronic cholangitis. Undoubtedly, chronic cholangitis is diagnosed largely on the basis of exclusion of other causes of latent icterus. Chronic infectious jaundice including that due to Leptospira icterohemorrhagica (spirochetal jaundice) offers many diagnostic difficulties. Spirochetal jaundice frequently is overlooked in this country. The various laboratory aids for identifying the causative agent afford the only reliable diagnostic criteria for spirochetal jaundice. Various other organisms occasionally may act as causative factors in chronic infectious jaundice.

4. Incipient spleen-liver disease, variously designated as splenic anemia or early Banti's disease, comprises a relatively definite group of latent icteric cases in our experience. We are familiar with the paucity of etiologic factors in this group of cases but clinically certain features seem to predominate. We have studied

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1. Thannhauser, J. S., and Anderson, E.: Bilirubin in the Blood Serum, Deutsches Arch. f. klin. Med. **137**: 179, 1921.

a number of cases in which the initial complaint was a massive gastrointestinal hemorrhage and in which subsequent studies failed to reveal evidence of definite gastric or duodenal ulceration. In some of these, in addition to slight hyperbilirubinemia, blood studies revealed varying degrees of thrombocytopenia, leukopenia and prothrombin deficiency. There usually, but not invariably, is a palpable spleen and the liver may show slight enlargement. Liver function studies may reveal impaired function. One of our patients in this group had several exsanguinating hemorrhages at yearly intervals. Splenectomy coincided with cessation of the hemorrhages, although the thrombocytopenia and leukopenia persisted. Follow up of the nonsplenectomized cases has not been fruitful. Some continue with mild hemorrhages. We do not believe that any of them developed into a full blown cirrhotic stage of so-called late Banti's disease.

5. There finally remain a small group of cases with persistent hyperbilirubinemia of undetermined origin.

TABLE 1.—*Serum Bilirubin Values*

Serum Bilirubin Mg. per 100 Cc. of Blood	No. of Cases	Per Cent
0.2	861	46.9
0.3	345	18.8
0.4	209	11.3
0.5	87	4.7
Above 0.5	333	18.3
	1,835	100.0

TABLE 2.—*Hyperbilirubinemia*

Duodenal ulcer	31
Irritable duodenum	49
Colon disease	57
Miscellaneous	50
Liver dysfunction (including cholangitis and catarrhal jaundice)	57
Obstructive jaundice	89
	333

How large a percentage of cases is represented in this category will depend on the diagnostic elasticity of the clinician. For example, one who is fond of the diagnosis of chronic cholangitis may find that he has no cases of hyperbilirubinemia of undetermined origin. Our interest in this problem was stimulated by the fact that over a period of years we studied a group of patients with symptoms vaguely and in some cases strongly suggestive of duodenal ulcer in which mild hyperbilirubinemia persisted. We believed that estimations of serum bilirubin in all of our studied cases might prove of value. Because of this interest, the serum bilirubin was determined in a larger percentage of our office cases than was warranted by the suspicion of any abnormality referable to that test. In the past several years serum bilirubin determinations were performed on almost all our patients.

The present study comprises a group of private patients observed during the period from January 1930 to January 1942 in which serum bilirubin determinations were carried out.

The following technic [2] was used in the determination of the serum bilirubin:

Solution A: Dissolve 1 Gm. of sulphanilic acid in 15 cc. of concentrated hydrochloric acid in water and dilute to 1 liter.

Solution B: Dissolve 0.5 Gm. of sodium nitrite in water and dilute to 100 cc.

Diazo reagent: To a 10 cc. graduated cylinder add 5 cc. of solution A and 3 drops of solution B. Prepare fresh before each determination.

Saturated ammonium sulfate: In a bottle place 100 Gm. of ammonium sulfate and 100 cc. of water. Shake for some time to dissolve and use the supernatant fluid.

Standard cobalt solution: Weigh 2.161 Gm. of anhydrous cobalt sulfate or 3.92 Gm. of Co So4 : $7H_{20}$, dissolve in water and dilute to 100 cc. in a volumetric flask.

Standard series: To eight test tubes add respectively 10, 7.5, 5, 4, 3, 2, 1.5 and 1 cc. of the standard cobalt sulfate solution. To the last seven add the correct amount of water to make 10 cc. Stopper and label respectively 2, 1.5, 1, 0.6, 0.4, 0.3 and 0.2 mg. The standard tubes are labeled to read directly in milligrams of bilirubin considering the 1-4 dilution in the method.

Pipet into a 15 cc. centrifuge tube 1 cc. of serum and 0.5 cc. of diazo reagent. Mix. Stand three minutes. Add 2.5 cc. of 95 per cent alcohol and 1 cc. of saturated ammonium sulfate. Mix and centrifuge at a relatively high speed for five minutes. Remove the supernatant fluid and compare it with the standards in a test tube of the same size.

On the basis of this technic we had assumed that the majority of our normal serum bilirubin values occurred at or below 0.3 mg. per hundred cubic centimeters of blood. However, there occurred a sufficient number of instances in which values in excess of 0.3 mg. obtained that we believed it desirable to analyze all of our office cases in which serum bilirubin determinations were recorded during a twelve year period. Excluded were all isolated consultations in which no laboratory work was recorded or cases which were studied largely in the hospital. There remained a group of cases (3,782) which we regarded as having had a fairly complete study. Of the 3,782 cases, 1,835 (48.9 per cent) had one or more determinations of serum bilirubin. In cases with multiple determinations of serum bilirubin, the maximum value was used in this study. The serum bilirubin values in 1,835 cases were distributed as shown in table 1.

The 333 cases of hyperbilirubinemia (i. e. serum bilirubin in excess of 0.5 mg. per hundred cubic centimeters of blood) were distributed as shown in table 2.

In the group of 333 cases of hyperbilirubinemia (i. e. a value above 0.5 mg. per hundred cubic centimeters of blood) the maximum serum bilirubin values were distributed as outlined in table 3.

Of 3,782 cases comprising the total number reviewed, a diagnosis of duodenal ulcer was made in 641 instances. In 313 (48.8 per cent) of the 641 cases, one or more determinations of serum bilirubin were made. The serum bilirubin values in 313 cases of duodenal ulcer were distributed as shown in table 4.

It is evident that the general pattern of distribution of serum bilirubin values in the duodenal ulcer group was similar to that in the total group reviewed, an interesting observation in connection with those serum bilirubin values below 0.5 mg. but of no practical importance in comparing the serum bilirubin values above 0.5 mg., since the total group comprised some jaundiced patients with liver and biliary tract disease in which one would anticipate an elevated serum bilirubin.

The diagnosis of duodenal ulcer was entertained only in those cases in which the history, physical examination, gastric analysis and roentgenographic demonstration of a niche supported such a diagnosis. The group labeled irritable duodenum comprised those cases

2. Keller A. G.: Manual of the Biochemical Laboratories of the Graduate Hospital, University of Pennsylvania, 1934.

in which the clinical picture was not of sufficient clarity to warrant accepting as clearcut cases of peptic duodenal ulceration. While in some instances, undoubtedly, the exclusion of certain cases from the duodenal ulcer group was based on captious criteria, our general observations in this article might apply either to the duodenal ulcer or to the irritable duodenum group. The group labeled colon disease comprised all the cases in which any disorder referable to the colon was present, including malignant disease, polyposis, ulcerative colitis and irritable colon. The liver dysfunction group comprised all the cases of catarrhal jaundice, toxic hepatitis of all types, cholangitis and hepatic cirrhosis of nonobstructive origin. The obstructive jaundice group comprised those cases in which there was the common denominator of some factor or group of factors that gave rise to varying degrees of jaundice due to disease referable to obstruction to the outflow of bile from the biliary tract or associated structures. In the miscellaneous group we placed all the cases with diagnoses which were otherwise unclassified, such as malignant disease of the stomach, hypertension and hyperthyroidism.

Excluding 89 cases of obstructive jaundice from the 333 cases of hyperbilirubinemia, there remained 244 cases which were further analyzed in an attempt to segregate those cases in which persistent hyperbilirubinemia obtained. For convenience, the cases were subdivided into three categories:

A. Cases in which only one serum bilirubin determination was recorded, obviously cases in which the persistence of hyperbilirubinemia was not considered.

B. Cases in which hyperbilirubinemia was present at some time during the period of observation but in which subsequent determinations were within the normal range. We likewise included in this group some cases in which hyperbilirubinemia was present during the whole course of a short period of observation, cases which certainly could not be regarded as showing persistent hyperbilirubinemia. Three cases observed for short periods in the liver dysfunction group in which death occurred likewise are included in this group.

C. Cases studied over variable periods during which all of the serum bilirubin determinations fell within our defined range of hyperbilirubinemia.

Accordingly, the 244 cases of hyperbilirubinemia were grouped as shown in table 5.

TABLE 5.—*Groups of Cases of Hyperbilirubinemia*

	A	B	C
Duodenal ulcer	23	4	4
Irritable duodenum	20	17	12
Colonic disease	32	17	8
Miscellaneous	26	12	12
Liver dysfunction	22	26	9
	123	76	45

Thus there were 45 cases of persistent hyperbilirubinemia in which no clinical evidence of obstructive jaundice could be demonstrated.

The following analysis was made of the cases of persistent hyperbilirubinemia under each of the main diagnostic headings:

1. *Duodenal Ulcer.*—Only 4 instances were noted in which persistent hyperbilirubinemia obtained in the duodenal ulcer group. The range of serum bilirubin values varied from 0.6 to 1.6 mg. (1 case in which five serum bilirubin determinations over a period of five years varied from 0.8 to 1.5 mg. showed 0.3 mg. on one occasion). In each case the cholecystogram showed a normally functioning gallbladder without evidence of calculi. Repeated bile drainage failed to demonstrate either calcium bilirubinate pigment or cholesterol crystals. In 2 cases the liver edge could be palpated on deep inspiration. A splenic enlargement was absent in all instances. Routine blood studies failed to reveal any hematologic abnormality. The urinary urobilinogen frequently was determined in each case and in no instance was the value any greater than a dilution of 1 to 30. In 1 case four bromsulphalein determinations (2 mg. per kilogram dose) over a five year period varied respectively as follows: 20, 10, 0 and 7 per cent retention in thirty minutes. In no instance has there occurred any other clinical or laboratory evidence which might explain the persistent hyperbilirubinemia.

2. *Irritable Duodenum.*—Twelve instances were noted in which persistent hyperbilirubinemia obtained in the irritable duodenum group. The range of serum bilirubin values varied from 0.6 to 2 mg. In 8 cases a cholecystogram was obtained which showed a normal gallbladder without stones in 5 cases. In 3 cases the cholecystogram showed a faint gallbladder shadow. In 10 cases one or more bile drainage examinations failed to demonstrate calcium bilirubinate pigment or cholesterol crystals. Many of the bile drainages showed evidence of moderate catarrh and exfoliation of the

TABLE 3.—*Maximum Serum Bilirubin Values in Cases of Hyperbilirubinemia*

	Serum Bilirubin, Mg. per 100 Cc. of Blood												
	0.6	0.7	0.8	0.9	1.0	1.1 to 1.5	1.6 to 2.0	2.1 to 3.0	3.1 to 5.0	5.1 to 10.0	10.1 to 20.0	Above 20.0	Total
Duodenal ulcer	12	5	4	3	1	4	2	..	..	..	..	..	31
Irritable duodenum	18	3	6	3	5	11	3	..	..	..	..	..	49
Colon disease	27	11	10	1	3	5	..	..	..	..	..	..	57
Miscellaneous	17	4	10	3	7	7	1	..	1	..	..	..	50
Liver dysfunction	9	2	6	1	7	4	8	4	5	5	3	3	57
Obstructive jaundice	21	8	8	1	7	9	5	7	9	9	3	2	89
Total	104	33	44	12	30	40	19	11	15	14	6	5	333

TABLE 4.—*Serum Bilirubin Values in Cases of Duodenal Ulcer*

Serum Bilirubin Mg. per 100 Cc. of Blood	No. of Cases	Per Cent
0.2	161	51.4
0.3	64	20.4
0.4	39	12.4
0.5	18	5.7
Above 0.5	31	10.1
	313	100.0

biliary tract in the recovered material. In 1 case giardiasis was noted. In only 1 case was the liver edge palpable on deep inspiration. A splenic enlargement was absent in all instances. Routine blood studies failed to reveal any hematologic abnormality. The urinary urobilinogen was present in normal concentrations in each case on many determinations. Bromsulphalein retention tests were carried out in 8 cases. In 3 cases respectively 10, 6 and 5 per cent retention of bromsulphalein was noted, in 1 of which the bromsulphalein was zero at a subsequent examination. In 1 case three bromsulphalein determinations were reported 15, 10 and 2 per cent retention. Whether or not we are dealing with a case of early hepatic cirrhosis is not clear in the 1 case with a consistently positive bromsulphalein retention, although it seems unlikely because the other clinical and laboratory findings are within the normal range. Not 1 of our hyperbilirubinemia cases in either of the duodenal categories has shown any evidence either of definite or of progressive hepatic damage.

3. *Colon Disease.*—There were 8 cases in which persistent hyperbilirubinemia obtained in this group with primary colonic disease. The range of serum bilirubin values varied from 0.6 to 1.5 mg. In 7 cases a cholecystogram was obtained which was normal in 4 cases; in 1 case the cholecystogram showed a faint shadow, in 1 case the gallbladder was sluggish and in 1 case there was a slight mottling in the gallbladder shadow. In the last case the collateral clinical and laboratory data did not support a diagnosis of cholelithiasis. Biliary drainage was done in 5 cases and, although at times the recovered material from the duodenum contained some exfoliative débris, no calcium bilirubinate pigment or cholesterol crystals were reported. In 2 instances the liver and splenic edges could be palpated on deep inspiration but there was no great increase in the size of either organ. In 4 cases the bromsulphalein dye retention test was performed, in 3 of which no retention was reported; in 1 case 8 per cent dye retention was noted. In 7 cases repeated determinations of the urinary urobilinogen were reported within normal concentrations.

4. *Miscellaneous.*—There were 12 cases in the miscellaneous group in which persistent hyperbilirubinemia was present. Of these, 2 presented blood dyscrasias (primary macrocytic anemia and hemolytic icteroanemia) which could account for the hyperbilirubinemia. Two other cases present isolated findings (1 showed calcium bilirubinate pigment in the material recovered from the duodenum by biliary drainage and the other case showed a negative defect in one film of a cholecystographic series) not inconsistent with a diagnosis of cholelithiasis but in which the other clinical and laboratory studies failed to confirm the presence of gallstones. There remained only 8 cases in which consideration was given to unexplained hyperbilirubinemia. In 2 of the cases no cholecystograms were recorded; of the remaining 6 cases, 2 showed sluggish gallbladders and in none was there any evidence of cholelithiasis. Biliary drainage was attempted in 4 cases, 3 of which showed some flocculent débris suggesting catarrh, 1 showed giardiasis and in none were either calcium bilirubinate pigment or cholesterol crystals recovered in the duodenal material. The bromsulphalein retention was normal in the 3 cases tested. One case showed urobilinogenuria in the dilution of 1 to 30; the other cases were all reported 1 to 20 or less.

5. *Liver Dysfunction Group.*—There were 9 cases in the liver dysfunction group with persistent hyperbilirubinemia, all of which might be segregated under the heading of chronic cholangitis. In these cases we were dealing with certain intangibles in which persistent hyperbilirubinemia was the only common finding. In table 6 the essential data are tabulated. Attention is directed to the length of the periods of observation, in one instance fifteen years. The serum bilirubin values in each case appear to range within definite limits without wide variations. The values for brom-

TABLE 6.—*Liver Dysfunction Group*

Case	Period of Observation	Number of Serum Bilirubin Determinations	Range of Serum Bilirubin Determinations	Bromsulphalein, per Cent Retention	Galactose Tolerance, Gm.	Urobilinogen Concentration	Bile Drainage	Palpable Liver	Palpable Spleen	Cholecystogram
B. F.	5/30 to 10/33 (3½ yrs.)	9	0.7-1.5 (1 test 0.4)	Not done	10/32 = 3.0 10/33 = 1.8	1-10	Adequate B catarrh exfoliation	0	0	Normal
J. L.	9/32 to 10/34 (2 yrs.)	27	1.0-3.2	Not done	10/32 = 3.1 1/33 = 4.2 5/33 = 2.5 1/34 = 2.6	1-20	Adequate B catarrh exfoliation	0	0	Not done
M. L.	7/34 to 6/41 (7 yrs.)	9	1.0-1.6	2/38 = 6	10/34 = 1.3	Not done	Adequate B (few cholesterol crystals once, 2/38)	Slight	0	Normal
W. M.	12/31 to 6/32 (6 mos.)	10	0.6-1.0 (2 tests 0.5)	Not done	2/32 = 1.7	1-10 to 1-30	Adequate B catarrh exfoliation	Slight	0	Not done
C. P.	11/33 to 12/38 (5 yrs.)	38	0.8-2.6 (1 test 0.4, 1 test 4.0)	12/34 = 0 9/36 = 12 12/36 = 0	12/33 = 1.4 3/34 = 0.6	1-20	Adequate B catarrh exfoliation	0	0	Normal
C. R.	4/32 to 7/33 (15 mos.)	6	0.8-2.0 (1 test 0.4)	Not done	Not done	1-10 to 1-40	Scant B catarrh exfoliation	2 inches below costal margin	0	Slender functioning G. B.
D. C. R.	3/30 to 5/30 (2 mos.) (previous jaundice for 2 yrs.)	4	1.3-2.7	3/30 = 5	Not done	1-60 to 1-80	Adequate B catarrh exfoliation	Slight	0	Normal function; suspicious negative shadows
A. S.	3/27 to 5/42 (15 yrs.)	15	0.6-1.6 (2 tests 0.5)	11/38 = 12 1/42 = 10	1/29 = 0 2/33 = 1.5	1-20	Adequate B catarrh exfoliation	0	0	Normal
C. W.	11/33 to 6/34 (7 mos.)	21	0.6-1.8 (1 test 0.4, 2 tests 0.3)	Not done	1/33 = 2.4 2/34 = 2.0	1-20 to 1-40	Adequate B catarrh exfoliation	0	0	Sluggish

sulphalein retention do not indicate extensive liver damage. The urobilinogen figures are not indicative of any progressive hepatic disease. The bile drainages universally showed evidence of biliary catarrh and exfoliation, similar to those which B. B. Vincent Lyon [3] attributes to cholangitis of varying degree. In no instance was the spleen palpable and in only 1 case was the lower margin of the liver easily felt. The cholecystograms were variable but in general indicated adequate gallbladder function. In 1 case the roentgenologist was unwilling to exclude cholelithiasis; however, the other clinical and laboratory evidence failed to support a diagnosis of calculus disease.

COMMENT

A survey of the foregoing material suggests the following:

1. Hyperbilirubinemia of moderate degree is frequently encountered in gastrointestinal patients.

2. The most obvious cause of hyperbilirubinemia is obstructive jaundice.

3. In cases in which obstructive lesions of the biliary system can be excluded, one must search for other factors which might give rise to jaundice.

4. There exists a small group of cases with idiopathic persistent hyperbilirubinemia lasting, in some instances, over a period of years, in the absence of obvious etiologic factors.

5. In our series there were no instances of pronounced delayed hepatic changes associated with persistent hyperbilirubinemia.

Some of the limitations of the value and validity of the observations recorded in the presentation might be noted:

1. Of 3,788 cases studied, serum bilirubin determinations were made in 48.9 per cent. The clinical suspicion that some serum bilirubin abnormality might be present in only approximately one half of our cases immediately introduces a large variable. A similar series of 3,788 cases in each of which a serum bilirubin determination was made would offer more accurate data. Serum bilirubin determinations on a similarly large group of normal persons would offer still more evidence on the range of values in normal persons.

2. The number of cases in which repeated serum bilirubin determinations were made is too small to offer any valid data concerning the range of normal values in any given group of patients.

3. Careful studies by other investigators on the range of normal serum bilirubin values indicate variations due to certain technical difficulties with the test itself. The relation of concentrations of serum bilirubin to serum proteins introduces a large variable. Mindful of these limitations, we believed that a review of our experience with the test as performed in private practice might prove of some value. Apparently abnormal serum bilirubin values occur frequently in the routine study of office patients. The clinician must assume the responsibility either of ignoring such values or of attempting to determine their etiology.

CONCLUSIONS

1. Hyperbilirubinemia may be due to obstructive jaundice, hemolytic jaundice, toxic hepatocellular disease and incipient liver-spleen disease. In a small group of cases idiopathic hyperbilirubinemia must be considered.

2. A review was made of 1,835 cases in which one or more serum bilirubin determinations were recorded.

3. Serum bilirubin values in excess of 0.5 mg. per hundred cubic centimeters of blood were termed hyperbilirubinemia.

4. The distribution of the serum bilirubin determinations indicated that 18.3 per cent of the serum bilirubin values were above 0.5 mg. per hundred cubic centimeters.

5. The distribution of the hyperbilirubinemia values was determined in our cases of duodenal ulcer, irritable duodenum, colon disease, miscellaneous disease, liver dysfunction and obstructive jaundice.

6. Further consideration of the clinical and laboratory data in association with persistent hyperbilirubinemia indicates that in a small group of cases followed over a period of years mild hyperbilirubinemia obtains in the absence of hematologic or obvious progressive hepatic disease.

3. Lyon, B. B. V.: Nonsurgical Drainage of the Gall Tract, Philadelphia, Lea & Febiger, 1923.

THE CLINICAL PREVENTION AND DIAGNOSIS OF LIVER DYSFUNCTION

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CHICAGO

Liver disease and liver dysfunction are becoming increasingly prevalent. It is now known that any chronically deficient diet may lead eventually to liver disease.

The American dietary is reported deficient in the vitamin B complex. One might assume that the recent enthusiasm for the intake of concentrated vitamin preparations might have counteracted this. However, two factors have nullified to a large extent the possible beneficial effect of increased vitamin intake: 1. Concentrated vitamin preparations are relatively expensive, and those who can afford to take them get an adequate amount in their diet, anyway. 2. A large proportion of commercial preparations do not contain the whole vitamin B complex—are apt to be rich in thiamine and nicotinic acid but poor in the other factors. There is some evidence to show that this disproportion can do harm as well as good. The desire for "sylphlike" figures has undoubtedly induced lowering of the carbohydrate intake. Man has enough carbohydrates or sugars in reserve to last only about one-half day. A certain amount of carbohydrate is essential in the diet if one is to avoid abnormal use of body fat. The hyperlipemia brought about by deficient carbohydrate intake leads to deposition of fat in the liver, producing fatty cirrhosis. Therefore, not only is the glycogen reserve of the liver depleted but the fatty replacement impairs normal liver function. Since an important function of the liver is detoxicating, toxic substances passing into it from the digestive tract may damage it further, owing to lowered local tissue resistance. These substances may even pass into the general circulation, where in turn they set up tissue changes which interfere with normal metabolism and may even lead to retrogressive changes. One may postulate that some of the noninfective types of arthritis may be related to this pathologic function.

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Read before the joint meeting of the Section on Pathology and Physiology and the Section on Gastro-Enterology and Proctology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

The coexistence of gallbladder disease and hepatitis forms another interesting situation. Many physicians believe that cholecystitis and cholelithiasis produce liver damage which may reach an advanced degree. This is especially true in persons who have acute episodes of suppurative gallbladder disease repeated at intervals.

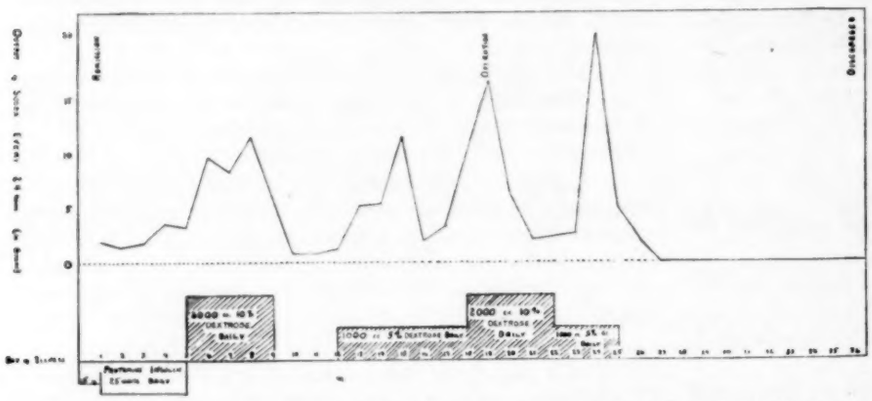

Fig. 1.—Effect of cholecystectomy on the daily urinary sugar output by a patient with hepatic damage and glycosuria who had received insulin at the outset and intravenous dextrose without insulin later.

Therefore, unless there is a definite contraindication which may add to the morbidity and mortality associated with surgical intervention, it may be wise to remove a calculous gallbladder to prevent liver damage. Certainly, when there is little surgical risk, I can see no good reason for failure to remove a pathologic gallbladder. In addition, the subgastric acidity and achlorhydria that may develop without operation lead to a lowering of the bactericidal activity of the gastric juice. This may promote the development of flora in the upper part of the jejunum and duodenum which may be a factor in ascending infections to the liver and lead to additional liver damage. Therefore, more accurate evaluation of disease of the gallbladder may be an important factor in removing a source of continued liver damage and allow the normal reparative processes of this organ to go on unhampered.

The effect of various diets on liver damage has recently been investigated by Earle [1] and others. They found that feeding rats a diet containing 10 per cent cystine leads rapidly to portal necrosis and hemorrhage and that prolonging such feeding produces cirrhosis of the liver. The type of diet definitely modified the mortality rate and the character of the lesion. Diets high in fat increased the severity of hepatic damage, while diets high in carbohydrate and protein and low in fat increased the number of mitotic figures indicating regeneration. Similarly, György [2] concluded that hepatic injury and fatty infiltration are definitely determined by dietary factors. He found that the addition of thiamine and riboflavin to the diet is of value in reducing the incidence of hepatic damage and that a diet low in casein and moderate to high in fat regularly induces hepatic injury after one hundred to one hundred and fifty days. The use of choline seemed to reduce the incidence of hepatic damage, and the addition of yeast was even more effective in preventing liver injury.

One should not look too lightly on jaundice and hepatitis in its incipient stage and pass it off as a supposed "catarrhal jaundice." Too often the disease may pass beyond clinical control and serious or fatal damage occur.

1. Earle, V. J.: J. Exper. Med. **75**: 179-189 (Feb.) 1942.
2. György, Paul, and Goldblatt, Harry: J. Exper. Med. **75**: 355-368 (April) 1942.

DIAGNOSIS

Liver dysfunction may be exceedingly difficult to diagnose and in many cases is masked by other clinical syndromes. The loss of appetite, morning nausea, biliousness, constipation, sudden attacks of or prolonged weakness on the least exertion, a tendency to perspire easily, loss of weight, sallow complexion, furred tongue, headaches and vertigo were known to older clinicians as evidences of liver disease. Today the newer knowledge of liver function may establish scientific criteria for old clinical truisms. Jaundice may be below the level for objective clinical manifestations and demonstrable only by serum bilirubin tests. Blood studies usually reveal an increased amount of serum bilirubin (latent jaundice). Liver function tests are discussed elsewhere in this symposium; but the most accurate tests may be negative in the presence of liver disease, or one may be positive while others give results within normal limits.

I should like to call attention to one form of liver disease that is not commonly recognized. Until a better name is given, it might be called the "cholecystohepatohyperglycemic and glycosuric syndrome." This is seen after treatment over long periods for true diabetes. The clinical picture is striking. Usually there is a long-standing history of gallbladder disease, interspersed in most cases with attacks of acute or subacute suppurative cholecystitis. Usually the gallbladder is not visualized. The sugar tolerance is not that of true diabetes but is more like that of liver damage. The urine contains sugar. Ketone bodies are not present and, as a rule, the physician makes a diagnosis of diabetes mellitus. Rarely if ever are there attacks of diabetic acidosis. The patient is usually given insulin, even large doses of protamine zinc insulin, with a presumed diabetic diet. In spite of this supposed adequate control

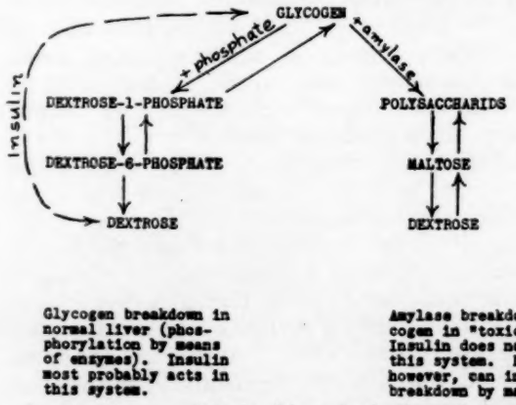
GLYCOGEN
+ phosphate
+ amylase
Insulin
DEXTROSE-1-PHOSPHATE
POLYSACCHARIDS
DEXTROSE-6-PHOSPHATE
MALTOSE
DEXTROSE
DEXTROSE
Glycogen breakdown in normal liver (phosphorylation by means of enzymes). Insulin most probably acts in this system.
Amylase breakdown of glycogen in "toxic" liver. Insulin does not act in this system. Dextrose, however, can inhibit the breakdown by mass action.

Fig. 2.—Diagram of the breakdown in the liver of glycogen to sugar (glycogenolysis), which is faster than its storage (glycogenesis).

the urine continues to show sugar. Blood studies may reveal high values, even as high as 250 mg. per hundred cubic centimeters, depending on the age of the patient and the duration of the disease. This was seen in 1 of the 6 cases that I observed.

REPORT OF CASE

Mrs. A. S., aged 66, entered the hospital April 22, 1940 with an immediate complaint of a more or less constant dull ache in the right upper quadrant of the abdomen for the previous

two weeks radiating to the left upper quadrant as well as in the opposite direction and into the back. She vomited several times. This subsided after limitation of her diet. She had lost 5 to 6 pounds (2.3 to 2.7 Kg.) recently. She had been constipated but noted no change in the color of her stools. She had been treated for many years for diabetes. Twenty years before she had had a presumed cholecystectomy. She had seven children and had ceased menstruating twenty years before. The rest of her history was not significant.

The patient looked her age on physical examination. Her blood pressure was 150 systolic and 70 diastolic, her temperature 99.2 F., her pulse rate 90 and her respiratory rate 20. There was no scleral icterus. The mouth was edentulous but otherwise normal. Aside from a systolic murmur at the base, the heart showed no unusual changes. The lungs showed evidence of moderate emphysema. There was an ancient scar in the right upper quadrant of the abdomen; exquisite tenderness was present in this region and a large mass was felt here, apparently connected with the liver, and this was also tender. The spleen was barely palpable.

The clinical diagnosis was recurring gallbladder disease in a patient who presumably had had a cholecystectomy twenty years before.

Wassermann and Kahn reactions of the blood were negative. The blood count showed erythrocytes 4,380,000, hemoglobin content 70 per cent (Sahli) and leukocytes 21,000, with a differential count of neutrophils 82 (stab cells 16 and segmental forms 66), 1 eosinophil, 15 monocytes and 2 transitional cells. Blood chemical analysis showed 244 mg. of sugar, 64 mg. of nonprotein nitrogen and 1.4 mg. of creatinine per hundred cubic centimeters. The icteric index was 5. Total cholesterol was 193, esters 94 and free cholesterol 99 (47 per cent esters).

The feces were brown and soft with no occult blood. The urine showed no albumin; there were occasional white cells and 0.2 per cent sugar (total for twenty-four hours, 2 Gm.). The flat film revealed a large gallbladder containing multiple radiolucent stones.

The patient had been receiving from 15 to 25 units of protamine zinc insulin daily for five days in the hospital previous to my seeing her.

I was curious about the abdominal mass so I immersed the patient in a tub of warm water to relax the abdomen. At this time the mass was found to be definitely connected with the liver and was either a firm enlarged gallbladder or Riedl's lobe.

The clinical picture resembled that of recurring suppurative cholecystitis with liver damage, and I therefore advised immediate cessation of insulin therapy. The diet was kept at 200 Gm. of carbohydrate, 50 Gm. of fat and 75 Gm. of protein (her weight was 50 Kg.). She was then given daily 200 Gm. of 10 per cent dextrose in water intravenously. While the urinary sugar output definitely increased (shown in the table), ketone bodies were not present in the urine, and even with the large amount of intravenous dextrose a gradual reduction occurred in the amount of sugar spilled over into the urine. The level of the blood sugar also eventually came down sharply, in spite of intravenous administration.

Fourteen days after this therapy was instituted the patient was considered to be in good enough condition for surgical operation. An empyema of the gallbladder with multiple stones; multiple adhesions of the gallbladder to the hepatic flexure, transverse colon, duodenum and omentum, and a dilated common duct were seen. Cholecystectomy with exploration of the common duct was performed, but there were no stones in the duct. Recovery was uneventful and, finally, with the same diet and without insulin, sugar was not spilled in the urine after the intravenous dextrose was discontinued. This is illustrated in figure 1 and the accompanying table.

Clinical Course of Patient with Hepatic Damage and Glycosuria *

Date	24 Hr. Urine Output, Cc.	Sugar, per Cent	Sugar, Gm.	Protamine Zinc Insulin, Units	Blood Sugar	Liver Function, Cholesterol Esters, per Cent	Comment
8/22†	1,020	0.20	2.0	15	244	0	
8/23	720	0.20	1.44	25	0	47	
8/24	900	0.20	1.8	25	0	0	
8/25	900	0.40	3.6	25	0	0	
8/26	1,620	0.20	3.24	25	0	0	
8/27	1,920	0.50	9.6	0	0	0	2,000 cc. of 10% dextrose in saline solution
8/28	2,880	0.30	8.4	0	0	0	2,000 cc. of 10% dextrose
8/29	2,880	0.40	11.5	0	0	0	2,000 cc. of 10% dextrose intravenously
8/30	3,300	1.20	40.3	0	230	0	2,000 cc. of 10% dextrose intravenously
8/31	960	<0.10	<0.90	0	0	74	Intravenous dextrose omitted
9/ 1	480	0.20	0.96	0	0	0	Intravenous dextrose omitted
9/ 2	660	0.20	1.3	0	0	0	Intravenous dextrose omitted
9/ 3	1,320	0.40	5.2	0	193	0	1,000 cc. of 5% dextrose intravenously
9/ 4	1,380	0.40	5.4	0	0	0	1,000 cc. of 5% dextrose intravenously
9/ 5	1,920	0.60	11.5	0	0	0	1,000 cc. of 5% dextrose intravenously
9/ 6	2,340	<0.10	<2.0	0	172	0	1,000 cc. of 5% dextrose intravenously
9/ 7	1,020	0.20	3.20	0	0	0	1,000 cc. of 5% dextrose intravenously
9/ 8	2,210	0	0	0	0	0	1,000 cc. of 5% dextrose
9/ 9	2,400	0.7	16.8	0	0	0	2,000 cc. of 5% dextro e; cholecystectomy
9/10	1,560	0.4	6.20	0	0	0	2,000 cc. of 5% dextrose
9/11	1,140	0.2	2.2	0	0	0	2,000 cc. of 5% dextrose
9/12	780	0	0	0	0	0	2,000 cc. of 5% dextro e
9/13	1,260	0.2	2.5	0	0	0	1,000 cc. of 5% dextrose
9/14	3,150	0.7	2.00	0	0	0	1,000 cc. of 5% dextrose
9/15	960	0.5	5.00	0	0	0	1,000 cc. of 5% dextrose
9/16	960	0.2	2.00	0	0	0	Intravenous dextrose discontinued
9/17	450	<0.1	0	0	0	0	
9/18	930	0	0	0	0	0	
9/19	600	0	0	0	0	0	
9/20	690	0	0	0	0	0	
9/21	600	0	0	0	0	0	
9/22	690	0	0	0	0	0	
9/23	300	0	0	0	0	0	
9/24	540	0	0	0	0	0	
9/25	360	0	0	0	0	0	
9/26	1,140	0	0	0	0	0	

* The patient throughout the period was on a 1,500 calory diet.
† Admission.

COMMENT

Other patients subjected to cholecystectomy showed essentially the same clinical picture. The best explanation of what is going on in the liver is brought out in figure 2. The breakdown in the liver of glycogen to sugar (glycogenolysis) is faster than its storage (glycogenesis).

Since insulin further depletes the storage of glycogen by the liver, owing to its deposition of sugar in muscle tissue, it increases the glycogenolytic process in the liver. The liver is further damaged when its protective mechanism of glycogen reserve is lowered. The hyperglycemia induced by the intravenous dextrose therapy prevents the rapid glycogenolytic manifestation: The process is reversed; the liver therefore stores more glycogen, the blood sugar level during fasting is lowered, the urinary sugar disappears and no evidence of "diabetes" other than the elevated blood sugar level, if that could be called evidence, remains. In some cases, with the improvement in the storage of glycogen other liver function returns nearly to normal, the blood sugar level returns nearly to normal and no urinary sugar is ever present after cholecystectomy, in spite of continuing the diet used before, with no insulin used at any time in the period studied.

This series of cases serves to emphasize apparently unrecognized liver dysfunction treated as diabetes. The

accurate scientific evaluation of this symptom complex and subsequent cholecystectomy substitute a life of well-being for one of invalidism and continued medical care.

The liver may be a factor in many obscure metabolic phenomena, and more investigations and studies should be directed along these lines.

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THE CONCEPT OF LIVER DEATHS

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In 1922 following a rather prolonged period of clinical observation it became evident that there were certain types of mortality that followed operations on the external biliary system.[1] There were three types of death that followed gallbladder surgery. Later these findings were more formally presented as follows:

GROUP 1.—Liver deaths associated with hyperpyrexia and coma. Death ensues in eighteen to thirty-six hours.

The first group is composed of patients who have had a comparatively simple gallbladder operation. The patients were usually obese and gave a history of chronic gallbladder disease. Preoperative study did not reveal any contraindication to surgical intervention. Following cholecystectomy the recovery from the anesthesia was slow; in fact, the patient never did emerge fully from the anesthesia. In four to six hours after the return to the ward the patient was in a semicomatose state that passed rapidly into stupor and coma, with a rapidly ascending temperature to 105-106 F.

GROUP 2.—Liver deaths associated with a constantly diminishing jaundice and the secondary development of stupor and coma, the final clinical picture similar to a "cholemic death" in cirrhosis of the liver.

The second group is essentially different in its clinical manifestation. The patients have had a chronic, severe type of biliary duct infection with obstructive jaundice and usually have had a previous cholecystectomy. The common duct obstruction has been relieved by drainage of the common duct and the postoperative condition of the patient has been somewhat but not completely satisfactory. After a variable period, four to seven days, the patient falls into a stupor, oliguria develops and the patient dies in coma with hyperpyrexia.

GROUP 3.—Liver deaths associated with and complicated by a secondary renal degeneration of severe degree.

The third group lacked two essential clinical features of the first two groups. There was an absence of the hyperpyrexia and coma. The patients within this group have had a chronic, severe type of gallbladder and duct disease. Forty-eight hours after operation there was a distinct vasomotor collapse and a continuous and increasing degree of oliguria, with a pronounced elevation of the nonprotein nitrogen. Anuria finally dominated the clinical picture, with death. This third group embraces the dual caption of hepaticorenal syndrome.

It was realized at that time that there was no authoritative foundation for these clinical syndromes except that based on clinical observation. The following factors, however, were apparent: 1. Postmortem examinations uniformly revealed no adequate cause for death except such associated changes as were incident to the age of the patient. 2. Most of these patients had a relatively good body chemistry before operation and nearly all of them had had adequate preliminary preoperative laboratory studies which indicated that there was no basic defect in kidney function. 3. This group of patients were gravely ill and the majority of them died. 4. All of these patients developed major renal complications if they survived long enough. Group 3 always developed varying degrees of oliguria which preceded the final development of an almost complete anuria. 5. The clinical status of the patients exhibited all gradients of severity. 6. The hyperpyrexia group invariably died in coma as the result of a fulminating toxemic process. 7. The ultimate mechanism of death, I believed, was a chemical disturbance within the liver. In my earlier experience the type of mortality under discussion was confined entirely to patients who were operated on for disease of the gallbladder or biliary tract, and the phrase "liver deaths"[2] was coined to express this concept.

In an evolutionary sense the liver is, with the exception of the primitive gastrointestinal tube, the oldest physiologic organ. The liver is able to protect itself and does so continuously from almost every type of intoxication whether introduced through the gastrointestinal tract or distributed through the vascular system. In some way or other the liver is concerned with practically every function in the body. It is an interesting and arresting thought that this organ, which under the ordinary conditions of life is so adequately endowed for the protection of the organism, fails if and when it must combat the by-products of the degeneration of its own cells. The mechanism that the liver exercises for the protection of the body apparently fails when the toxins are of hepatic origin. The condition undoubtedly has its origin in the degeneration of individual liver cells. If the process is acute, fulminating, there is a very early death with hyperpyrexia and coma: "liver death." If the process is less severe and the elaboration of the hepatic toxins less rapid, the patient survives until the secondary effects of this toxin are manifest in destruction of renal parenchyma with the clinical picture of oliguria, progressing to anuria; hence the associated mechanism of liver-renal damage—the hepaticorenal syndrome.

On a few occasions it has been noted that in crushing injuries of the liver there was a clinical picture of hyperpyrexia with coma and death. The importance of this fact was not recognized or given emphasis until 1927, when a case was reported of a young woman who had a grave injury to her liver following an automobile accident.[3] This was followed by hyperpyrexia within the first twenty-four hours and death. Postmortem examination revealed that the cause of death could not have been hemorrhage and that there was a traumatic necrosis of liver tissue with a high degree of parenchymatous degeneration of the cortex of the kidneys—hepaticorenal syndrome.

Another very interesting observation was the degree of liver damage associated with intra-abdominal infec-

Read before the joint meeting of the Section on Pathology and Physiology and the Section on Gastro-Enterology and Proctology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

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2. Heyd, C. G.: "Liver Deaths" in Surgery of the Gallbladder. J. A. M. A. **97**: 1847-1848 (Dec. 19) 1931.

3. Furtwaengler, A.: Diffuse Rindennekrose beider Nieren nach Leberruptur (Ein Beitrag zu den angiopastischen Krankheitsbildern in der Chirurgie), Krankheitsforschung **4**: 349-374 (June) 1927.

tions.[4] The mechanism of liver damage was by either the portal system or the intrahepatic bile canalicula and in patients presenting any degree of such liver damage there was almost always an associated change in the capsule of Glisson, with the laying down of fibrous tissues capable of being demonstrated as white, opaque areas over any or all portions of the liver, more particularly in the area extending out from the gallbladder fossa.

Significant experimental work was done by Boyce,[5] who prepared various emulsions of liver tissue from patients dying of this complication; he demonstrated that alcoholic extracts of such liver tissue when injected into dogs did not produce the complication and aside from some slight indispositions in his animals no bad results obtained; on the contrary, when an aqueous solution was injected into animals, parenchymatous degeneration of liver cells with similar changes in the convoluted tubules of the kidney was found. This picture in the experimental animals exactly simulates the picture obtained post mortem in patients who die of the hepaticorenal syndrome.

It is also interesting that clinical pictures identical with those originally described have been reported as arising with or without surgery and in conditions other than those associated with operations on the biliary apparatus. It is also advanced by competent observers that the basic mechanism in these liver deaths is a fulminating, overwhelming infection. Careful examination of the evidence submitted by the proponents of this idea fails to carry with it sufficient reasonableness as to make it acceptable.

Gross traumatic necrosis of liver cells or some unknown mechanism of injury of liver cells may produce an extremely powerful toxin as the result of necrosis of liver cells, and this in turn exercises a specific effect on all parenchymatous tissue and more particularly on the epithelium of the convoluted tubules. The toxin, if such it is, does not arise per se in the kidney but arises in the liver, and the renal sequelae are the end result effected by the excretion of foreign protein.

In group 1 the patients who died in eighteen to twenty-four hours with hyperpyrexia and coma did so because of an overwhelming toxemia and they did not live long enough to develop what I believe to be the inevitable secondary renal changes. The persons in the other two groups were able to sustain life for a longer period than in group 1, with the result that on autopsy they invariably exhibited the secondary changes in the renal tubules in the form of cloudy swelling and necrosis. It is this peculiar chemical sequence that gives rise to the hypothesis that while the liver has the most extraordinary ability to protect the organism from injury arising from the gastrointestinal tract, through the portal circulation, or from injury coming to it via the systemic circulation, it does not have the same ability to protect itself from necrosis of its own liver cells, and the absorption of the by-products of liver necrosis will lead to death in a relatively short time with hyperpyrexia and coma or a death of later sequence when liver degeneration is associated with degeneration of the kidney.

116 East Fifty-Third Street.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DR. MANN, DRS. MATEER, BALTZ, MARION AND MACMILLAN, DRS. JOHNSON AND BOCKUS, DR. PORTIS AND DR. HEYD

DR. CHESTER M. JONES, Boston: If Dr. Mann's observations can be transferred from animal experimentation to human beings, the fact of selective diversion of material from the portal stream in various types of liver is of extreme importance, and it may help to explain the fact that the oral tests of liver function differ distinctly from the results obtained when material is given intravenously. It is quite possible that comparative values between two such methods will be of real help. Dr. Mann implied the wisdom of putting the liver under strain either by exercise or by the intake of food in order to obtain the most definitive results in covering the function. The factor of safety of this organ is so great, it is perfectly obvious in minor changes that no liver function test gives any information, but if one puts extra strain on the organ the minor differences may be brought out. The insistence of Dr. Mateer and his collaborators on finding normal figures cannot be overemphasized. The fact that there are wide variations within the normal has been too generally overlooked. Drs. Johnson and Bockus say that 0.5 mg. of bilirubin per hundred cubic centimeters may not represent an abnormal figure. Certainly it is unwise to carry out too fine distinctions when minor differences may well fall within normal limits. Liver function tests are not diagnostic; they are not yet delicate enough. Their chief value is that they confirm a clinical diagnosis or determine progress. The surgeons are using large amounts of sulfonamide compounds intraperitoneally, and no doubt the rapid absorption of these through the portal system at times produces serious liver damage, which may complicate the operation for which the patient came. One effect is a dangerous prolongation of the prothrombin time. In some cases there is jaundice in addition. When the portal blood flow is interfered with either by fibrosis, as occurs in cirrhosis, or by other conditions in which the liver is damaged, the powers of repair are damaged. Because of interference with portal blood flow, ascites may develop. This is not the case and I think it should be stressed definitely that ascites is an evidence of liver failure rather than of increased portal blood pressure and is due fundamentally to hypoproteinemia.

DR. J. P. SIMONDS, Chicago: Dr. Mann's approach to the study of the liver through the door of morphology is interesting and significant. It should be borne in mind that the liver and every organ in the body perform their functions through the medium of a specific structural pattern. Morphology, or structure, is therefore the foundation for a complete study of the effects of disease on any organ. The structural modification induced in any organ by disease will obviously influence its function. The functional disturbances that accompany disease can be adequately understood only if they are studied in connection with the characteristic structural changes. Amebic abscesses of the liver are far more common in the right than in the left lobe of this organ. On numerous occasions I have observed atrophy of the left lobe of the liver, particularly the portion of it that lies to the left of the falciform ligament. It would be interesting to know whether there is any relation between this localized atrophy and the streamlining of the circulation through the liver. Dr. Mateer and his collaborators have rightly emphasized the need of more reliable standards for tests of hepatic function. Dr. Mann not only has made clear the reason why standards need to be revised but also has furnished the reason for variation in results of such tests when the test material is given in different ways. It is significant also that in a paper now in press Hepler and Gurley have shown that there is a close correlation (correlation coefficient as high as 0.875) between the weight of the patient and the quantity of benzoic acid excreted as hippuric acid. In this test there is no rigidly fixed standard, but results for any patient must be evaluated in connection with his weight.

DR. HENRY A. RAFSKY, New York: Abnormal liver function tests in persons below 60 years of age may be normal for persons above this age range. The age factor should be taken into account. Dr. Newman and I have made a study of various

liver function tests. We studied the cholesterol partition, cephalin flocculin tests, bromsulphalein and oral and intravenous hippuric acid tests in a group of so-called normal persons above 60 years of age. In nearly all of the subjects thus far studied at least one test was positive. In reference to Dr. Portis's mention of vitamin B_1, we found porphyrinuria comparatively frequently in these persons of normal age. A woman of 53 gave a history of having consumed much alcohol for many years, loss of weight and intestinal bleeding. The liver was enlarged and the hemoglobin was 57 per cent. Cancer of the intestinal tract was ruled out. On proctoscopic examination, with the instrument inserted to a depth of 6 inches, varicosities were noted. This finding is not often emphasized as confirmatory evidence of the presence of cirrhosis of the liver. These varicosities, in conjunction with the clinical and laboratory data, made the diagnosis of cirrhosis of the liver a certainty. This simple diagnostic procedure might be helpful in suspected cases of cirrhosis especially when they do not present a typical textbook picture.

DR. MOSES PAULSON, Baltimore: The interpretation of abnormal liver function tests in nonsurgical patients without jaundice and without clinical evidence of liver disease as indicative of early or occult hepatic disturbances of clinical significance should be accepted with great caution. Under the conditions set forth the tests themselves are open to question. Controls—with one exception by Mateer—have been done with single, not with multiple, tests and chiefly in the young; almost always, in suspected disease multiple tests are employed and usually in older persons. When in the control study using multiple tests Mateer encountered unexpected hepatic dysfunction, he discounted such results as being falsely positive because of too sensitive tests. This may or may not be so. Occult hepatic dysfunction or subclinical hepatitis as indicated by abnormal liver function tests have been reported in peptic ulcer, rheumatoid arthritis, skin disorders, neuroses and psychoses. Wyler and I have found that more than 64 per cent of those with dyspepsia without historical cause for liver disease had hepatic dysfunction by at least one of two or more tests used. I used to think that abnormal tests were significant under these conditions, indicating occult hepatic dysfunction of subclinical hepatitis, until this study was completed. When we consider this widespread evidence of liver dysfunction as determined by tests and compare it with the relative infrequency of clinical hepatitis or cirrhosis, several questions arise. Do the tests actually measure liver dysfunction under the circumstances referred to? Are not some of the tests already too sensitive? If the tests actually measure liver dysfunction, does it not seem that such information is not of great import in view of what rarely happens, namely liver disturbance of clinical significance? What has been said is not to be confounded either with tests used in confirmation of clinically evident liver disease or to determine its progression or regression, or in the differential diagnosis of jaundice.

DR. JOHN G. MATEER, Detroit: Most of our normal control individuals, studied with the various newer liver function tests, ranged between 25 and 35 years of age. There were a few persons included in this normal group who were between 35 and 45 years. I am not surprised that Dr. Rafsky found a tendency toward the development of positive liver function tests in elderly persons involving at least some functional impairment of the liver, since other organs and organic systems also tend to deviate from normal in elderly persons. The all important point to emphasize regarding liver function tests is that they should be interpreted properly. We believe that they should always be interpreted only in relation to the clinical, x-ray and other laboratory findings if a reasonably accurate total diagnosis is to be attained. We also believe that, in the determination of the normal standard for any test by the study of normal control individuals, one should be conservative and allow a margin in drawing the line of demarcation between normal and abnormal. We do feel that there is a practical advantage in determining the lesser degrees of impaired liver function, which are not associated with permanent, serious and persistent liver disease. One of the best illustrations of this point is found in the gallstone cases referred to in our paper. It is certainly an advantage to know before operation which of these cases present impairment of liver function, so that the benefit of special preparation for operation may be given.

DR. THOMAS A. JOHNSON, Philadelphia: We anticipated Dr. Jones's thought about the matter of the level of serum bilirubin which we accepted as representing hyperbilirubinemia. I should go further and say that the van den Bergh reaction is entirely unreliable in that range and that photoelectric cell determinations of direct serum bilirubin are more accurate.

DR. SIDNEY A. PORTIS, Chicago: Dr. Mann's discussion regarding the repair of liver damage taking place through the arterial rather than the portal system supports the contentions of those who maintain that intravenous therapy is far superior to that given by mouth. This is especially true in disturbances of glycogen metabolism. One cannot get sufficient concentration in the portal vein at any one time to be of benefit in liver damage, while the hyperglycemia produced by intravenous dextrose is sufficiently high to spill over the increased threshold to nourish the liver cell. The series of patients that I have presented have been treated for a long period of years as diabetic, with insulin and diet, and still could never be made sugar free. A more careful evaluation of these patients revealed that we were dealing with liver damage manifested by increased amylolytic activity in the liver cell which was caused by disease of the gallbladder. Therefore the withdrawal of insulin, the giving of intravenous dextrose and subsequent cholecystectomy brought about a return to near normal in their sugar metabolism. I agree with Dr. Jones and have seen some untoward reactions from the indiscriminate use of sulfonamide compounds. I should like to call Dr. Paulson's attention to the fact that we are not dealing with end results but with subclinical disease, and we hope by these manifestations and tests to prognosticate what might later happen to a patient. Many patients with obscure gastrointestinal symptoms may have occult liver disease without noteworthy objective findings. We should investigate the possibility of hepatitis, and treatment should be instituted long before outspoken liver disease has developed in order to prevent irreparable damage.

DR. DWIGHT L. WILBUR, San Francisco: Dr. Jones raised the question of the incidence of parasitism, and particularly of infection with liver flukes, among the patients who came under our observation. We found infection in only 1 case; the parasite was Ascaris lumbricoides. There are many problems in relation to the geographic distribution of primary carcinoma of the liver and particularly to the frequency of it among Chinese, Japanese, Filipinos and members of the Bantu and certain races of South Africa which remain to be solved and which may give significant information regarding the etiologic or predisposing factors of the disease. Undoubtedly in certain parts of China the high incidence of the disease is due to infection with the liver fluke. In other countries the incidence of parasitism is identical in patients who have primary carcinoma of the liver and those who do not have it. It is not unlikely that in Japan the widespread use of "butter yellow," a dye used to color butter, may account for the high incidence of the disease, for it is well known that in the experimental animal this substance is definitely carcinogenic. The importance of dietary deficiency as a predisposing factor of primary carcinoma of the liver is not clear, but in experimental animals it may be an important factor predisposing to the disease.

DR. VIRGIL H. MOON, Philadelphia: One feature discussed by Dr. Heyd deserves more emphasis. I too have seen that hepatorenal syndrome, the so-called liver deaths, and have been keenly interested in their mechanism, not as related to liver injury, but as related to another syndrome, that of shock. These patients die with the shock syndrome characteristically manifested clinically, and the characteristic pattern of visceral pathologic changes is seen post mortem. A highly important item is the evidence of renal insufficiency among those patients who lived several days. It is now recognized that shock occurs in varying degrees and with varying severity. Those with shock of maximal degree may die promptly or within twenty-four hours, those with shock of minimal degree may recover; but the intermediate group in which a sublethal degree of shock persists over a period of time regularly manifest progressive renal insufficiency. Observations and studies on this point will be published soon.

SUBDURAL HEMATOMA AND EFFUSION AS A RESULT OF BLAST INJURIES

SECOND PRELIMINARY REPORT
DIAGNOSIS BY PSYCHIATRIC EXAMINATION

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In this series of 10 patients with subdural hematoma and effusion due to blast, definite neurologic findings have been infrequent or minimal. As a result, some of the patients had repeatedly been considered to have a "functional" condition, and such diagnoses as "psychoneurosis," "war neurosis" and "traumatic neurosis" had been made. Several had been classified as having "postconcussional" states.

Should this practice be general, it is evident that many will be medically discharged from the armed services with relatively curable organic lesions. The social aspects of such a situation are extremely important, to say nothing of the damage to the personality, future adjustment and earning power of any such patient. He will be considered as "neurotic" or "shell shocked" and in his disabled condition may well become a public charge. Furthermore, it is probable that prolonged presence of a subdural hematoma or effusion will result in permanent cerebral changes and mental deterioration.

It is therefore imperative that every possible facet in our diagnostic armamentarium be exhausted to rule out the presence of these conditions in patients who have been exposed to blast. In our experience, careful psychiatric examination with the use of specialized psychologic testing has been more successful as an indication for pneumoencephalography than the usual neurologic criteria.

PSYCHIATRIC EXAMINATION

The clinical picture presented by these organic cases is different qualitatively from psychoneuroses with anxiety hysterical states. In the latter, extreme restlessness, motor activity, subjective tension, nightmares and insomnia are prevalent. Loud noises, sounds of airplane motors and exhaust explosions are "triggers" sending them into profound anxiety. Objectively, they may demonstrate signs of sympathetic overstimulation with hyperventilation, tachycardia, vasomotor flushing, dilated pupils and cold, moist and discolored extremities. Intellectual impairment is not present, as demonstrated by various test procedures.

The subdural cases, to the contrary, present one of two syndromes. In the most frequent syndrome, there is rather pronounced retardation in intellectual activity and personality interrelationships. The facies is one of dulness with but little play of facial expression. The emotional tone has the "feel" of dulness or vacuousness. The attention, during the interview, is impaired and the response times are slow. Answers to questions are remarkably barren in description and detail. The whole approach to life situations, as exemplified by the dynamics of the interview situation, is one of superficiality and attempt to "get by" without complicated mental activity. These patients are not dramatic in their assertions of headaches and other complaints.

The most graphic characterization might be made in the terms of pressure or "push." Patients with subdural lesions are noted for complete lack of push and initiative, whereas patients with an anxiety or traumatic neurosis give the impression of nearly overwhelming pressure. The former may state day after day that they have a headache but register no particular surprise nor make requests for attention when treatment is not given. The contrast of the neurotic, with the intensity and demanding air of his complaints, is well known.

The less frequent syndrome occurs in those cases of longer duration and demonstrates the more classic picture usually associated with the organic reaction types. The most striking feature is the impairment of inhibition or restraint producing a euphoric and sometimes facetious air. Motor restlessness with exaggerated mannerisms and gesticulations may be prominent. The emotional tone has the raw "feel" of the organic type with lability and explosiveness. Vasomotor flushing of the face and increased neuromuscular tension can be seen as somatic evidence of quickly stimulated rage reactions. The voice is too loud for the size of the room or for the distance between the examiner and the patient, and laughter is stimulated frequently by the patient's own remarks. The patient may assume unusual liberties in the interview situation, demonstrating poor judgment in interpersonal relationships. Undue productivity, unusual expressions of hostility, self aggrandizement and frequent reminiscences may be part of the lack of restraint.

Definite organic intellectual defects in the form of distractability, memory failure, perseveration and repetition, circumstantiality and "overparticularization," or too much attention to unimportant details may be present. A mild motor aphasia with hesitation on certain words or with difficulty in repeating test phrases may support the impression of organic brain disease.

USE OF PSYCHOLOGIC TESTING

The routine means of gross psychologic testing may suffice in many instances, particularly when correlated with the clinical picture that has been described. The ability to perform complicated calculations may or may not be impaired and care must be used in adjusting the degree of complication to the original level of intelligence and attainment. The recall of digits forward may not be impaired, as several patients who had other prominent organic characteristics were able to return eight digits. The reversing of digits, however, represents a higher order of cerebral activity and is likely to furnish added evidence in favor of an organic syndrome. For instance, the recall of eight digits forward and only three in reverse represents an inconsistency. The ability for subtraction of sevens from one hundred serially is but slightly impaired in some cases. The organic element may manifest itself by fatigue, with one or two mistakes near the end of the procedure.

Probably more important than the actual figures obtained on the foregoing testing is a qualitative analysis of the patient's performance. Slow response times, poor powers of concentration and emotional upset with rage reaction when confronted with failure may point toward an organic condition.

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SPECIALIZED TECHNICS

Rorschach Test.—The Rorschach studies are as yet incomplete and dilation of this method of diagnosis is planned for the future. However, this technic can be an excellent diagnostic aid in borderline and puzzling cases. A fairly characteristic picture is expected in the "dull" syndrome similar to the findings in intracranial tumors by Harrower-Erickson.[1] In differential diagnosis the anxiety and conversion neuroses are likely to give a typically neurotic performance with color shock, lack of human movement and the predominance of animal movement over human movement. Intellectually, production is likely to demonstrate some degree of balance between whole and detail responses. The subdural cases, however, demonstrate a lowered productivity with from eight to fifteen responses predominantly of the popular, "easy" whole variety. There is little attention to detail and no particular color shock. A previously well adjusted personality may be suggested by several good human movement and form-color responses. Interpretatively the performance can be characterized as a superficial, rather vague adjustment with little drive toward an analytic survey of the environment. Reduced productivity and originality go along with the lack of initiative and "push" mentioned before, rather than an absolute dearth of ideation as a careful testing of the limits will demonstrate. In those with impairment of restraint, a more classic organic picture may be obtained with gross impairment of abstraction demonstrated, although the degree of impairment necessary to produce five or more of Piotrowski's [2] signs of organic brain disease is seldom expected.

SHIPLEY-HARTFORD RETREAT TEST FOR INTELLECTUAL IMPAIRMENT [3]

The most useful single instrument has been the Shipley-Hartford Retreat test for measuring intellectual impairment. The ease of administration, scoring and interpretation make it ideal for the military conditions of limited psychiatric personnel. A corpsman can be trained to administer and score the tests with little loss of time by the medical officer.

A complete description of the test with theoretical considerations and methods of standardization has been published by Shipley,[4] Shipley and Burlingame [5] and Pollack.[6] The vocabulary test gives an estimation of the original intelligence, as this faculty is not readily affected by organic brain disease. The test in abstraction requires not only actual intellectual preservation for success but also attentiveness and some drive for accomplishment.

In this total of 10 cases, 9 demonstrated conceptual quotients in the direction of intellectual impairment, as shown in table 1. It will be noticed that only one, patient 9 (J. P.), attained a conceptual quotient above 100, and analysis of the scores indicates that his whole level of performance, including vocabulary, is impaired. A total mental age of 12.1 is not in keeping with his former level of adjustment and his rating as corporal. The two officers with conceptual quotients of 93 were considered on close analysis to be in the direction of impairment because of extremely superior intellectual backgrounds above their abstraction mental age of 16.5.

Generally, from our experience with these and other subdural hematomas not due to blast we are convinced that the Shipley test is more sensitive to pathologic conditions of the frontal lobe. On the basis of normal abstractive ability we have been able to speculate correctly in advance that a pathologic condition did not seriously involve the frontal lobes.

TABLE 1.—*Results of Tests in Ten Cases*

Patient	Diagnosis	Vocabulary	Abstraction	Total	Vocabulary Mental Age	Abstraction Mental Age	Total Mental Age	Conceptual Quotient
1. H. F. H., S2/c	Bilateral subdural effusion, frontotemporal area	20	12	32	13.1	11.0	11.5	83
2. W. C. C., Pfc.	Bilateral subdural effusion, frontotemporal area	32	22	54	17.8	13.6	15.9	76
3. R. T. C., Cpl.	Subdural effusion, right frontotemporal area	33	10	43	18.2	10.5	13.7	50
4. R. T. G., Pfc.	Subdural effusion, left temporoparietal area	32	28	60	17.8	15.7	17.1	88
5. H. A. P., F1/c	Bilateral subdural effusion, frontotemporal area	20	8	28	13.1	9.9	10.9	74
6. C. M. D., S2/c	Subdural effusion, left frontotemporal area	8	6	14	?	9.4	8.6	?
7. E. M. P., Lt. Cmdr.	Right subdural hematoma; left subdural effusion, temporal area	38	30	68	20.2	16.5	18.4	93
8. C. S. M., Lt.(j.g.)	Subdural hematoma, left frontotemporal area	34	30	64	18.6	16.5	17.8	93
9. J. P., Cpl.	Bilateral subdural effusion, frontotemporal area	17	18	35	11.9	12.5	12.1	104
10. C. N. G., WT 1/c	Subdural hematoma, left, with ventricular shift	33	24	57	18.7	14.2	16.5	80

In the aforementioned cases a comparison of preoperative and postoperative examinations reveals that 4 patients have made complete recovery as gaged by the conceptual quotient, while 1 has improved. Others have been operated on too recently for evaluation.

Some caution must be used in evaluating the significance of pathologic conceptual quotients. It must be certain that the patient has exercised due effort in taking the test. Other conditions in this age group, such as schizophrenia and severe depression, often demonstrate a low conceptual quotient, but these are usually eliminated easily by clinical study. In differentiating between organic injury and neurotic states there should be no serious discrepancies in the latter between the vocabulary level and the ability to perform abstractions. In cases similar to case 9, in which the impairment is so great that all the scores are very low, a comparison should be made between the mental age level and the previous adjustment, life attainments and education. Such a patient is likely to have other striking abnormalities on psychiatric examination.

REPORT OF CASES

CASE 3.—R. T. C., corporal, U. S. M. C., demonstrates the "dull" syndrome. This patient sustained shrapnel and other wounds from blast injury while in action against the enemy in the Pacific area. He was unconscious for an indefinite period of time and "hazy" for several days. Following improvement from the shrapnel wounds he continued to complain of

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2. Piotrowski, Z. A.: The Rorshach Ink Blot Method in Organic Disturbances of the Central Nervous System, J. Nerv. & Ment. Dis. **86**: 525-537 (Nov.) 1937.

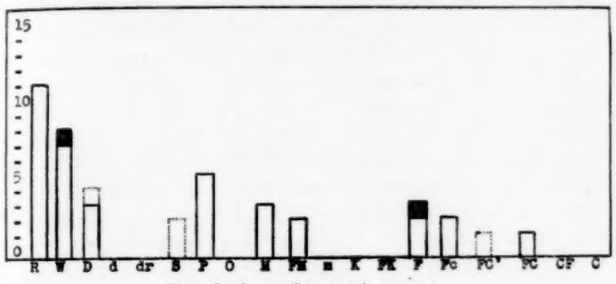
3. Test material furnished by courtesy of the Neuropsychiatric Institute of the Hartford Retreat, Hartford, Conn., Dr. C. C. Burlingame, Director.

4. Shipley, W. C.: A Self-Administering Scale for Measuring Intellectual Impairment and Deterioration, J. Psychol. **9**: 371-377 (April) 1940.

5. Shipley, W. C., and Burlingame, C. C.: A Convenient Self-Administering Scale for Measuring Intellectual Impairment in Psychotics, Am. J. Psychiat. **97**: 1313-1325 (May) 1941.

6. Pollack, Benjamin: The Validity of the Shipley-Hartford Retreat Test for Deterioration, Psychiat. Quart. **16**: 119-131 (Jan.) 1942.

occipital headaches, dizziness, nervousness and nightmares. Nausea with vomiting was frequent, and a board of medical survey considered that he had a traumatic neurosis. He was therefore transferred back to the continent. Here physical examination demonstrated perforation of the right ear drum and multiple recent scars of high explosive wounds over various portions of the body. The only positive neurologic signs were bilateral nystagmus, a mildly positive Romberg sign and slight dysmetria on the left finger to nose test. On psychiatric



Rorschach psychogram in case 3.

examination he presented a facies of dulness with ideational retardation. His attentive powers were impaired. He developed a rage reaction when he found that he could not subtract sevens from one hundred serially. He could return only five digits forward and three in reverse. He attained an intelligence quotient of 98 on the Otis self-administering test, intermediate form A. This, compared with a vocabulary mental age of 18.2, an abstraction mental age of 10.2 and a conceptual quotient of 59, indicated a superior original intelligence with definite intellectual impairment.

The Rorschach psychogram is shown in the accompanying chart. The psychogram demonstrates the findings described before with low productivity, slow response time and an overemphasis of easy and popular whole responses. The personality configuration, although barren, is not that of a psychoneurotic condition. Three human movement responses and one form-color response in this setting give evidence of a previously well adjusted personality. Statistically there are only two of Piotrowski's signs of organic deterioration.

Pneumoencephalography revealed a filling defect in the right frontotemporal area with shift of the ventricular system to the left. Craniotomy by means of perforator opening in the right superior temporal area revealed a tense and blue dura. When this was incised, several ounces of old blood and yellow fluid escaped.

He has made an uneventful recovery. A Shipley-Hartford Retreat test performed ten days postoperatively revealed the results shown in table 2.

TABLE 2.—*Results of Shipley-Hartford Retreat Test in Case 3*

	Score	Mental Age Level
Vocabulary	32	17.8
Abstractions	24	14.2
Total	56	16.3

Conceptual quotient 80. This result is still in the direction of impairment but is evidence of improvement.

CASE 8.—C. S. M., lieutenant (j. g.), U. S. N. R., presented an example of the syndrome described with impairment of restraint. He was rendered unconscious for two hours by the explosion of a ship 100 yards distant, Dec. 7, 1941. After returning to consciousness he was confused and had a violent headache for several hours. As there was much work to be done, he forgot about his own difficulties and did not report for hospitalization. He experienced a questionable convulsive seizure on April 7, 1942 and was given a thorough clinical and laboratory study. Physical and neurologic examinations were negative. One medical officer noted that the patient seemed to be mentally confused. Spinal puncture revealed an initial pressure of 225 mm. of water, but total protein was 20 mg. per hundred cubic centimeters. Roentgenograms of the skull were negative. It was decided that a diagnosis of epilepsy was not justified on the evidence at hand, and the patient was returned to duty. He was again admitted for hospitalization on November 10 following definite convulsive seizures with tonic and clonic convulsions, tongue biting and postseizure confusion and weakness. Neurologic examination was again negative, the diagnosis of epilepsy was established and the patient was transported to this hospital for a pneumoencephalogram.

Here the patient again demonstrated a normal neurologic examination. He was definitely abnormal on psychiatric examination, however, and a positive diagnosis of organic brain syndrome could be made. He displayed pronounced hyperactivity with exaggerated mannerisms and gesticulations. Emotional lability was definite, a basic euphoria being quickly and momentarily replaced by rage reactions and depressions of mood. His restraint and judgment were greatly impaired, as demonstrated by his interpersonal relationships during the interview. His voice was too loud and he frequently laughed at his own remarks. Intellectually he was circumstantial and repetitious and demonstrated automatic phrasing. He dwelt on inconsequential reminiscences of his past. He gave a history of increasing impairment of concentration, memory failures and inadequacy in his work as an engineer. He expressed a feeling of insecurity because of his awareness of this inadequacy and general lowering of mental efficiency.

Although his conceptual quotient on the Shipley-Hartford Retreat test was 93, his abstraction mental age of 16.5 did not conform to his professional and previous university standing in subjects requiring exquisite abstractions. Pneumoencephalograms demonstrated a definite filling defect in the left frontal region. Surgical exploration revealed an old subdural hematoma in that area.

COMMENT

It is planned to present a complete clinical and psychiatric study of these and succeeding cases in the future. Follow-up studies will be made as practicable. Electroencephalography will be utilized as a further diagnostic aid when facilities permit.

SUMMARY

Early differentiation of subdural hematoma or effusion from psychoneuroses, traumatic neuroses and "postconcussional" states is important individually, socially and economically.

A careful psychiatric examination can demonstrate intellectual impairment in cases of subdural hematoma or effusion despite negative neurologic examination.

Intellectual impairment in blast cases with or without positive neurologic findings is an indication for a pneumoencephalogram.

The Shipley-Hartford Retreat test is an effective instrument in the diagnosis of subdural hematoma or effusion.

Indigestion in Later Life.—The arteriosclerotic patient has thickened vessels, often hypertension, and tardy digestion. The management of this type of indigestion is largely hygienic and dietetic, being calculated to relieve the burden of digestive work. The treatment of such a case would begin with a complete rearrangement of the diet, lessening protein intake and fats, and using foods which are readily digestible. Another type is found in the cardiac individual, particularly of the angina or coronary type on the one hand and the individual who has defective cardiac function with a tendency to decompensation on the other. These patients suffer from flatulent indigestion and large, indigestible meals which embarrass the heart and may produce an attack. Small digestible meals and particularly avoidance of a large liquid intake are the fundamental principles to be followed.—Rehfuss, Martin E.: Indigestion: Its Diagnosis and Management, Philadelphia, W. B. Saunders Company, 1943.

ROLE OF THE ANAL GLANDS IN THE PATHOGENESIS OF ANO-RECTAL DISEASE

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Medicine today has come to accept as rational therapeutics the surgical treatment of anorectal disease. This common acceptance of the application of local removal and drainage of diseased tissues in or adjacent to the bowel outlet is not limited to infective processes. One of the common rectal problems from the standpoint of diagnosis and treatment is fistula in ano. Fistulas occur in the various age periods with an increased incidence in adult life. The fact that it is always associated with some degree of abscess formation predicates the infective nature of this disease process. The tendency of this infective lesion to tunnel through the anorectal tissues, involving adjacent structures and following a multiplicity of patterns with more or less self-limited regional manifestations, but not always communicating with the bowel, stimulated our interest to make a further study of the anatomic background of this problem.

It has been surmised that the system of anal glands somehow acts as a predisposing factor in the production of infectious lesions which develop in the perirectal tissues. It has been presumed that the infection finds its way through the anal wall by way of these glands, however. The nature and extent of this glandular system has not been adequately studied, as shown by a survey of the literature dealing with the problem and of the textbooks concerned with its clinical and therapeutic aspects. Quite obviously, there is no clear conception as to the part played by these glands in anorectal disease. It is our purpose to present in this study the results of our investigation into the embryology and histology of this gland system and to point out the part that it plays in local disease processes.

REVIEW OF THE LITERATURE

Interest in the existence and function of the anal crypts dates as far back as 1732. At this time Winslow [1] recognized their presence and described them as "semilunar lacunae." About the same time (1738) Astruc [2] in his treatise on fistula in ano refers to the anal crypts as short ducts or lacunas which appear to convey a "viscid humor."

In 1888 Bodenhamer,[3] summarizing the observations of Coats (1841), Gibson (1850) and Gross (1856), described these anal crypts as being foramens and cavities with communicating follicles. These crypts, he claimed, when excited, irritated or chronically inflamed become relaxed, weakened, enlarged and elongated, thereby losing their contractile power and permitting foreign bodies to enter the pouches, thus favoring production of the disease in question.

It was not until the year 1914 that Franklin Paradise Johnson [4] published his monumental treatise on "The Development of the Rectum in the Human Embryo" and illustrated their structure and location by reconstruction. His studies laid the basis for our present knowledge on this neglected subject. He demonstrated the existence of anal ducts and their glands in the various stages of embryonic development.

More recently, however, Tucker and Hellwig [5] confirmed by examination of diseased tissue removed at operation and by study of embryos of representative vertebrates the constant occurrence of branched tubular ducts as "preformed" structures. These ducts did not seem to be the result of any process of degeneration but were presumed by these investigators to be the vestigial remains of large glands found in the lower animals. They assumed that the crypts of Morgagni were not by themselves responsible for the frequency of anal infection but that infection originated as a rule in preformed tubules which are called anal ducts.

Gordon-Watson and Dodd [6] refer to the anal glands as probably "vestigial" remains which "often lose their connection with the anal glands by obliteration of the ducts during development, and that in some instances when the duct is patent, infection from the anal canal takes place."

The recent observation by Robert Scarborough [7] of a primary carcinoma in the incomplete canalized or "rudimentary remains of the anal glands" served to focus our attention once more on this important problem.

MATERIALS AND METHODS

A microscopic study was made of the anal canals of 17 subjects: 1 seven month fetus, 5 newborn infants and 11 adults. The tissues from the fetal and newborn subjects were obtained at autopsy, while all specimens from adults were surgical, having been obtained in the course of resections of the colon incident to malignant growths located high in the rectum and sigmoid.

Complete serial sections through the anorectal region were prepared on specimens taken from 2 of the newborn infants, and from 1 of these a scale model (43 diameters) was constructed according to the Harrison method.[8] A second model (250 diameters) representing a further enlargement of a typical portion of the anal gland bearing area from that shown in the first model was fashioned in clay and cast in plaster. From all other specimens serial sections were made through the region of the anal crypts and those sections selected for study which showed the presence of anal glands.

OBSERVATIONS

In all 17 cases studied anal glands were found extending into the subepithelial tissues in the zone between the anorectal and the anocutaneous line. However, a wide individual variation was noted in the number of the glands, in their structural plan and in the depth to which they invaded the tissues. In the

From the Departments of Proctology and Microscopic Anatomy, College of Medical Evangelists. Aided by a grant from the Alumni Research Fund.

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newborn case in which the entire anal canal was modeled, more than fifty glands were found arising in this area.

An average gland may be described as having a duct which opens into an anal crypt. The duct is lined with a stratified epithelium the surface cells of which appear columnar with basally placed nuclei. Communicating with this duct are from one to six slender tubular structures lined with two or three layers of epithelium. These tubular portions of the gland may run either a straight or a spiral course extending either cephalad or caudad. Glands that extend cephalad from the site of their ducts are usually simpler in structure (unbranched tubules) than those which extend caudad. One adult had a gland which extended so far cephalad that its terminal portions reached past the anorectal line into the submucosa of the rectum (fig. 1). The glands usually penetrate only into the deeper portions of the submucosa, but in 2 cases in the series they were observed to extend into the substance of the internal sphincter (fig. 2). In 1 case the gland was found to penetrate three fourths of the thickness of this muscle. In this series they were not observed in tissues deeper than that of the internal sphincter.

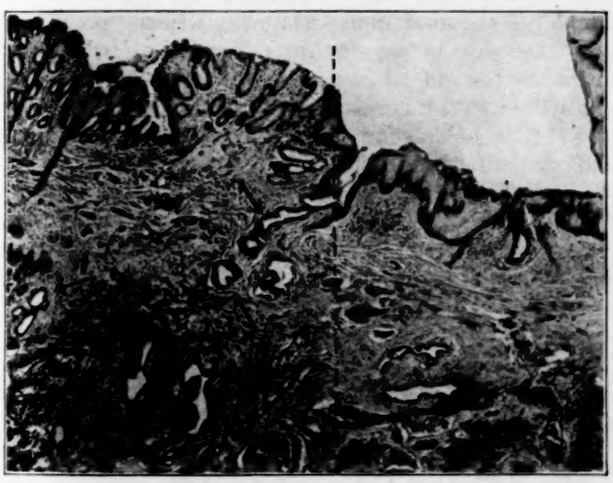

Fig. 1.—Cephalad extension of anal glands (arrows) beyond anorectal line (broken line); hematoxylin and eosin stain, × 19.

An interesting finding was the lack of complete canalization of the terminal portions of the anal glands in 3 of the newborn infants and an obvious cyst formation in 1 adult. In portions of the glands which were not canalized, the central part of the solid cord of cells often contained large polygonal squamous cells with very light staining cytoplasm. At the point at which the gland became canalized, the central light staining cells were seen to give way to a typical glandular type of lining epithelium with dark, basally placed nuclei. A careful examination of all the adult specimens failed to reveal any positive instances of uncanalized glandular structures. However, in several specimens the lumen of the gland was very small and eccentrically placed and seemed to branch rapidly in a fashion which closely resembled those glands from newborn specimens which were not completely canalized.

In 4 adult specimens the surface layer of the epithelium lining the ducts of the anal glands presented apical cytoplasmic vacuoles (fig. 3). The cells containing these vacuoles gave a positive test with Krajian's [9] carbolfuchsin stain for mucin. Another evidence of secretory activity of the anal glands was furnished by the finding already mentioned in 1 adult case of a cyst of the tubular portion of an anal gland (fig. 4). Since this observation was made accidentally in tissue that was being used for the perfecting of a special staining technic, it was impossible to find and

Fig. 2.—Anal glands (arrows) penetrating internal sphincter. Lower gland has extended three fourths of the thickness of the muscle; hematoxylin and eosin stain, × 19.

examine all portions of the serial section ribbon. However, in none of the 15 to 20 sections available could any connection with a duct be demonstrated. Additional evidence that this structure had possessed secretory function and had lost its connection with its duct was furnished by the fact that its lining epithelium was flattened and that it was definitely distended with coagulated fluid which stained positively with the mucin stain.

Another finding worthy of note was the presence of lymphocytes in the immediate vicinity of practically all

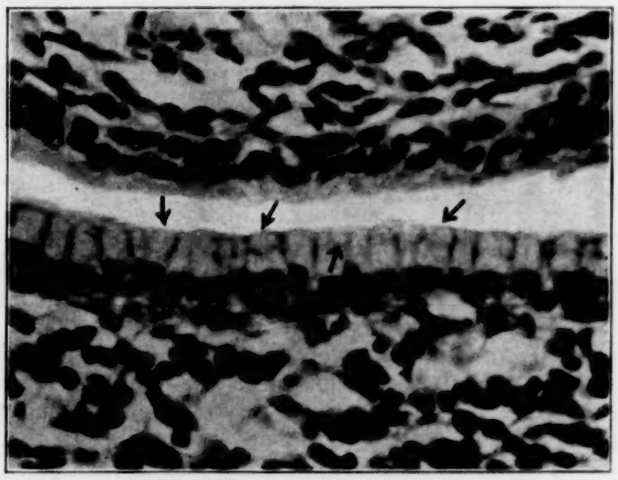

Fig. 3.—Epithelium of anal gland showing apical cytoplasmic vacuoles suggestive of secretory function; Krajian carbolfuchsin stain for mucin, × 520.

anal glands. In some specimens this lymphocytic infiltration was slight, whereas in others it was so pronounced as to suggest the structure of lymph nodules. In only 1 patient, an adult, were the lymphocytes found to have invaded the epithelial lining of a gland or its duct. The zone of lymphocytic infiltration that surrounded the anal glands and their ducts was continuous

9. Krajian, A. A.: Histological Technic, St. Louis, C. V. Mosby Company, 1940.

with that which occurred deep in the epithelium which lines the anal canal and when followed cephalad proved to be continuous with the diffuse lymphoid tissue of the tunica propria of the rectum and colon. Whether the presence of lymphocytes represented a response to an inflammatory process is a question which can be

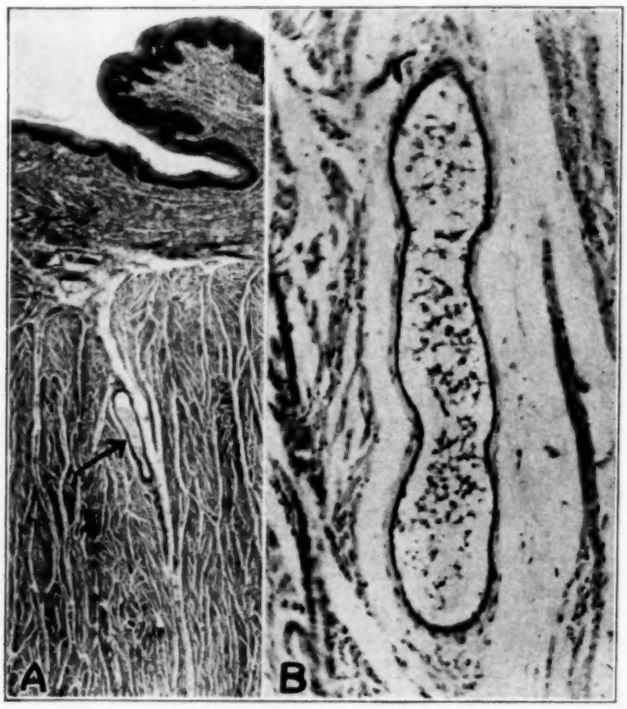

Fig. 4.—Cyst formation in anal gland showing *(A)* location of cyst in internal sphincter (hematoxylin and eosin stain, × 19); *(B)* enlarged view of cyst (Krajian carbolfuchsin stain for mucin, × 110).

answered in the negative on the basis of (1) the presence of some lymphocytes in all specimens examined, including those from the newborn, and (2) the absence of any significant number of polymorphonuclear leukocytes in the areas under consideration.

Particular attention was given to the presence of smooth muscle in the submucosa of the anal canal in the anal gland bearing area. In harmony with the findings of Fine and Lawes,[10] this study revealed the presence of smooth muscle in this area of the so-called pecten band in each of the 11 adult specimens examined. In 5 of the 11 cases, the band of muscle was very thick, in 2 it was relatively thin and in the remaining 4 it was intermediate in thickness. In 3 of the 11, small smooth muscle fasciculi were diffusely scattered among the larger strands of connective tissue, while in the remaining 8 the muscle fibers were more compactly arranged. In the newborn specimens, the smooth muscle of the submucosa of the anal canal was found to be in the process of differentiation, muscle cytoplasm being obvious only in scattered areas of the tissues.

CLINICAL APPLICATION

The constant occurrence of anal glands as emphasized by the studies of Tucker and Hellwig and confirmed by our study makes it reasonable to assume, as has been done in the past, that infection may be transmitted by the system of anal glands. The fact that there were such decided individual variations of the anal glands may explain why some persons seem to be more susceptible to anorectal disease than are others. In order to correlate the microscopic changes of anal glands with the development of anorectal disease, consideration must be given to the various successive steps involved in the disease process.

It is commonly recognized that any alteration in bowel habitus is responsible directly or indirectly for more pathologic conditions of the anorectal region than all other possible causes combined. Limited space will permit only a brief consideration of the various possible factors involved in these changes.

Simple traumatic lesions of the anorectal region are the result of an overdistention of the anal canal by the passage of dry or hard fectal matter. Conversely, it is also acknowledged that constant irritation following frequent loose evacuations for long periods will likewise produce a similar condition. This trauma, according to Lockhart-Mummery,[11] is most likely to occur in the posterior midline where the arrangement of the muscle fibers of the external sphincter give the least support. This being the weakest point of the anal orifice, any undue stretching is likely to occur at the posterior commissure, since the fibers supporting this region are not parallel to the anal wall. The next weakest point is at the anterior commissure, since relatively few circular fibers are present to give support.

Furthermore, it is recognized that the bowel tract acts as a natural habitat for the commonly known pathogenic and nonpathogenic bacteria. As previously mentioned, under certain stress and strain these organisms from the bowel may invade the adjacent tissues, namely the gland bearing area. In addition to this mode of bacterial activation and a weakened constitution, especially in the presence of disease elsewhere in the body, such as infected teeth or tonsils and disease of the upper respiratory tract, a decrease in tissue resistance is apt to occur which encourages or enhances the development of infection. Other avenues of activation which affect the gland bearing elements into a state of active localized cellulitis

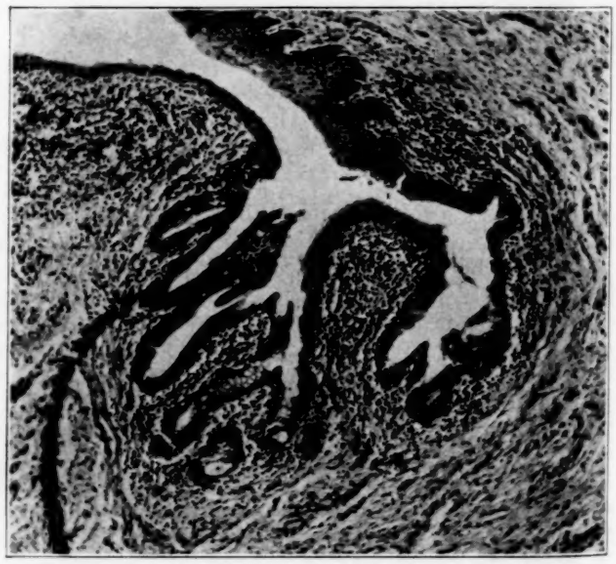

Fig. 5.—Enlarged deep crypt with numerous ramifying anal glands. Lymphocytes are infiltrated around the mucus producing glands. Hematoxylin and esosin stain; reduced from a photomicrograph with a magnification of 73 diameters.

10. Fine, J., and Lawes, C. H. W.: On Muscle-Fibers of Anal Submucosa, with Special Reference to Pecten Band, Brit. J. Surg. **27**: 723-727 (April) 1940.

11. Lockhart-Mummery, J. P.: Diseases of Rectum and Colon and Their Surgical Treatment, Baltimore, William Wood & Company, 1934.

may be brought about not only by direct invasion through the system of anal glands but also by way of the tissues developing as a result of a blood borne origin.

Under these circumstances an infective process would be expected to follow the lines of least resistance. Therefore, changes in contour, size and depth of the anal crypts, particularly those situated in the posterior midline or immediately on either side of this area, are more frequently found to become involved following continued irritation and trauma. Therefore, after infection has invaded the anal crypt its mode of spread and advance would follow a definite microscopic pattern.

One of our specimens (fig. 5) clearly demonstrates an enlarged and elongated crypt with numerous ramifying anal glands extending into the muscularis submucosae ani. It is obvious that infection, once set up by trauma or other irritation in such a crypt, could continue to spread along the avenues of all the glands present in this structural formation.

Another interesting observation (fig. 1) was that of several glands which were noted to extend cephalad beyond the mucocutaneous junction into the submucosa of the rectum. This finding offers a logical explanation of the occasional occurrence of abscesses and fistulas encountered in this region when the primary focus of infection is located in an anal crypt.

Similarly, the small, unbranched type of duct and gland with its shallow penetration pointing toward the lining of the anal canal in close proximity to the anocutaneous line gives satisfactory reason for the acute infected fissure which becomes chronic and unyielding to ordinary simple measures and which at the time of the operation proves to involve the regional anal crypt.

In the adult case represented in figure 2 the extent of invasion of an anal gland is seen to be deep penetration into the internal sphincter. Some authors have expressed the opinion that the glands may invade even the outer longitudinal muscle. This possibility, however, was not confirmed by our study. Should this penetration of glandular structures be along muscle bundles or fascial planes, it is reasonable to conclude that the zone of spread of infection would include those structures adjacent to this line of cleavage.

In the study of the fetal tissue, attention was called to two outstanding details, i. e. (1) uncanalized glandular structures and (2) a variation in the thickness of the submucosa and the retarded differentiation of the muscularis submucosae ani. These findings suggest two possible explanations for the occurrence in adult tissues of isolated, epithelium lined cystic formations. The formation of such cysts may be the result of either (1) failure of the cord of epithelial cells to canalize and communicate with its duct or (2) a choking off of certain glandular tubules which have previously invaded the area in which the fibers of the muscularis submucosae ani subsequently develop.

The findings noted in one of our adult patients of a cyst with flattened epithelial lining and distended with coagulated fluid which stained positively for mucin provides a basis on which may be explained the development of those abscesses and fistulas which do not communicate with the anal canal. The accumulation of fluid within this cyst (fig. 4) suggests that its lining epithelium possesses a glandular function. This assumption of glandular activity is further confirmed by the presence in 4 cases of cytoplasmic vacuoles in the epithelial cells of the anal ducts. Such isolated cysts may serve as a focus for the development of a blood borne infection in a manner similar to that which occurs in other parts of the body, such as the thyroglossal duct and cervical cysts. Trauma to such a cyst may conceivably predispose to abscess formation also.

It has always been perplexing and difficult to explain the existence of primary carcinoma when found in the perianal tissue. A recent case report by Scarborough [7] pertains to the possibility of primary carcinoma originating in an anal gland. It is conceded in this study that such a glandular cyst as shown in figure 4 might even serve as a nucleus for the development of a neoplasm.

Since the early part of the sixteenth century anatomists have made mention of a "viscid humor" secreted by the anal crypts, yet it has been quite impossible to uncover any literature of the microscopic picture of an anal crypt that demonstrates by special stain or cytologic procedure this particular function. Many authors discuss this matter, referring to the secretory function of the anal glands, particularly in animals,[8] and usually assume that the anal glands of the human being are vestigial.[6] The present study does not bear out the latter assumption. It has been suggested by local pathologists that these glands are active only at certain periods, a small number of glands being active at a given time. It is thus assumed that each gland is active by cycles. Special stains applied to the tissues from 3 of our patients gave positive evidence of the presence of mucin either in the cytoplasm of the epithelial cells or in the coagulated fluid adjacent to the epithelium. This observation suggests that these glands are not vestigial but are structures which function throughout life.

SUMMARY AND CONCLUSIONS

While some causal relationship between the anal glands, perirectal abscess and fistula in ano has been presumed to exist, the underlying and developmental and structural basis for this relationship has never been fully established. In this study we have investigated the structure, distribution and relationship of the anal glands in 1 seven months fetus, 5 newborn infants and 11 adults.

Anal glands manifested a wide individual variation as to number, depth of penetration and contour. Lack of complete canalization of the terminal portion of the anal glands was observed in 3 newborn infants. In some of the adult specimens the cells lining the anal glands presented apical cytoplasmic vacuoles which stained positive for mucin. The appearance of a cyst of the tubular portion of an anal gland further suggested a secretory function. The presence of smooth muscle in the submucosa of the anal gland bearing area was found to vary in thickness and in stages of development. Variable lymphocytic infiltration was noted in all cases studied and was considered of nonpathologic significance.

Various existing traumatic, bacterial and constitutional factors unite to permit infection to spread by way of the anal gland system. The extension of anal glands upward beyond the anorectal line into the rectal submucosa offers a logical explanation of the occasional occurrence of abscess and fistula in this region. The deep penetration of an anal gland seen extending into the internal sphincter points to possible avenues of invasion along muscle bundles, fascial planes and adjacent structures to these lines of cleavage. One adult had a definite gland cyst, which supports the claim that abscess and fistula may develop without communication with the anal canal. Primary carcinoma originating in

the perianal tissue is possible to occur, perhaps following chronic trauma, with a glandular cyst serving as a nucleus for development. The assumption that anal glands in the human being are vestigial remains and function only in animals was not supported by our observation. Instead, these glands are evidently active as secretory structures throughout life.

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ABSTRACT OF DISCUSSION

DR. ROBERT A. SCARBOROUGH, San Francisco: Owing to the microscopic nature of the anal glands, it has appeared reasonable to assume that infection pocketed in an anal crypt was the causative factor in the development of fistula in ano, since every such fistulous tract leads back to the site of such a crypt. This crypt is often of considerable depth, showing evidence of a chronic inflammatory process. It occasionally happens that a fistulous tract, as it is followed back from the secondary opening, approaches the epithelium at the mucocutaneous line but no actual surface opening can be grossly demonstrated. This has led in the past to some confusion concerning the origin of such fistulas. I have felt that such glands must be an important factor in the not infrequent development of fistula in ano in young infants, whose anal crypts are thin, delicate, healthy valves without the evidence of chronic infection found usually in this disease in adult patients. The authors' excellent microscopic studies in the newborn have served to support this belief. This paper has given us the first evidence of the secretory function of these glands.

DR. CLAUDE C. TUCKER, Wichita, Kan.: This demonstration of the presence of lymphocytes in the immediate vicinity of anal glands which had been shut off from anal ducts may be the answer to the origin of abscess and fistulas which do not communicate with the bowel wall. In our studies the ducts and crypts were excised from diseased tissue. In the past nine years we have studied from a histopathologic standpoint several thousand specimens and seldom did we find the wall of the ducts not diseased and oftentimes we found lymphocytes in the surrounding tissue. In second and third stage hemorrhoids the diseased ducts were found in the pile tissue. When all visible ducts and crypts have been removed at the time of operation, it is no indication that others may not become infected. Thus the infected crypt becomes edematous and the papillae become enlarged and sensitive. Many reflex symptoms are often produced from a single infected duct and crypt. Many of the so-called tumors arising at the anorectal line are simply enlarged papillae which have grown out of an inflammatory process which had its origin in an infected duct and crypt. Robert Scarborough reported a case of carcinoma with its origin in an anal gland. We also have had one originating in anal ducts, proving that these structures are not free from primary malignancy.

DR. MALCOLM R. HILL, Los Angeles: The results of our investigation were derived from anorectal tissues showing little or no pathologic change. The newborn subject was selected for model reconstruction in an attempt to make an accurate count of the number of glands present in the tissues of the anorectal canal. We were able to outline in detail the branched intramuscular glands but in addition to this many single unbranched gland structures. In both the infant and adult specimen studied there was noted a pronounced variation both as to location and as to the number of glands present. Lockhart-Mummery explains why daily or repeated trauma to the crypt line and these adjacent glandular structures is more prevalent in the posterior commissure and secondarily in the anterior anal margin by virtue of lack of support to the muscle structures. While the anal crypt is frequently the port of entry to the numerous ducts and glands, it must not be overlooked that the coexisting cryptitis may be secondary to a primary infection in the anal gland system. Blood borne infection to these gland bearing areas must not be overlooked. The isolated gland mentioned by Scarborough gives a ready explanation of the etiology of the abscess and fistula which has no direct continuity with the bowel. The cyst formation present in this type of glandular structure predicates the possible insurance risk from trauma in line of duty. Modern war surgery has been confronted with a similar analogy in the recurrence of a pilonidal cyst from experience in a jeep car or tank. Our study has not borne out the idea that these glands are vestigial remains. Secretory activity was shown to be present. Hirschman for years has taken cultures of the secretion or discharge from the anal crypt and found that the derived autogenous vaccine is a valuable therapeutic agent. This would lead one to conclude that the anal gland system is a potent field for focal infection.

MAPHARSEN IN THE TREATMENT OF CONGENITAL SYPHILIS

WITH ESPECIAL CONSIDERATION OF THE INTRAMUSCULAR METHOD OF ADMINISTRATION

GIRSCH D. ASTRACHAN, M.D.
AND
VAN ALSTYNE CORNELL, M.D.
NEW YORK

Mapharsen, which was studied and introduced by Tatum and Cooper,[1] was investigated clinically by O. H. Foerster, who made the first report on the use of this drug in antisyphilitic therapy for human beings at the meeting of the American Dermatological Association in 1933.[2] Since then numerous investigators[3] have published articles on the therapeutic efficacy of this drug as well as on its toxicity. Most of the investigators agree that mapharsen is a good antisyphilitic drug[4] and that it is less toxic than neoarsphenamine.[5]

The fact that only six fatalities[6] resulting from the use of mapharsen have been reported, while over

Miss Florence Ramsden, Dr. Leo Leibovitz and Dr. Israel Hirshon cooperated in looking up records and checking the after-effects of treatment.

Read before the Section on Dermatology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1942.

From the Department of Dermatology and Syphilology, and from the Department of Pediatrics, Metropolitan Hospital, and from the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

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3. Moore, J. E.; Hardy, S. M.; Robinson, H. M., and Eagle, Harry: The Response of Quantitatively Titered Wassermann Test in Early Syphilis to Treatment with Five Different Arsenical Drugs, Am. J. Syph., Gonor. & Ven. Dis. **20:** 503 (Sept.) 1936. Kulchar, G. V., and Barnett, C. W.: Mapharsen in the Treatment of Early Syphilis, ibid. **20:** 482 (Sept.) 1936. Gruhzit, O. M., and Dixon, R. S.: Mapharsen in Mass Treatment of Syphilis in a Clinic for Venereal Diseases, Arch. Dermat. & Syph. **34:** 432 (Sept.) 1936. Miller, H. E.; Epstein, N. N., and Simpson, R. G.: Mapharsen: Its Use in the Treatment of Syphilis, California & West. Med. **45:** 321 (Oct.) 1936. Wieder, L. M.; Foerster, O. H., and Foerster, H. R.: Mapharsen in the Treatment of Syphilis: Further Studies, Arch. Dermat. & Syph. **35:** 402 (March) 1937. Cole, H. N., and Palmer, R. B.: Mapharsen in the Treatment of Syphilis, ibid. **36:** 561 (Sept.) 1937. Astrachan.[15]

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12 million ampules of this drug have been manufactured,[7] makes this trivalent arsenical very suitable for antisyphilitic therapy.

The value of mapharsen in congenital syphilis was studied by us [8] as well as by Morgan,[9] Howles [10] and Wile [11] and fairly good results were reported.

The present paper deals with the problem of the efficacy of mapharsen in congenital syphilis, experimentation with larger doses and also the problem of local pain following the intramuscular administration of this drug.

Eighty-seven patients were treated, of whom 57 had late congenital syphilis, 11 early congenital syphilis and 19 latent syphilis (adult women in whom mapharsen injections were given intramuscularly). There were 36 cases from the Metropolitan Hospital division of the Welfare Island dispensary (service of Dr. Van Alstyne Cornell), 20 from the Metropolitan Hospital (services of Dr. Van Alstyne Cornell and Dr. Reuel Benson), 21 from the Skin and Cancer Unit (service of Dr. Fred Wise) and 10 from our private practice. Sixty-one patients were females, 26 males. The oldest among the congenitally syphilitic patients was 51 years, the youngest was 4 weeks. Altogether 1,742 injections were given (1,507 to congenitally syphilitic patients and 235 to adult patients with latent syphilis). The number of injections given intravenously was 1,012; the number of injections administered intramuscularly was 730. The dosages given to early congenital syphilitic patients ranged from 0.5 to 15 mg. The dosages in late congenital syphilis ranged from 2 to 30 mg. for children and from 10 to 60 mg. for adults.

TABLE 1.—*Effect of Mapharsen Therapy on the Serologic Reaction of Late Congenital Syphilis*

Total number of cases	56
Number of cases in which the serologic reaction was studied	45
Blood serologic reaction reversed partially or completely in	25 (55.5%)
Blood serologic reaction remained unchanged in	20 (44.5%)
Average number of mapharsen injections in improved cases	27.3
Average number of mapharsen injections in unimproved cases	20.1

EFFECTIVENESS OF MAPHARSEN THERAPY

Effect of Mapharsen Therapy on the Serologic Reaction in Late Congenital Syphilis (tables 1 and 2).—Fifty-six patients were treated and the serologic results studied of 45 patients. They received an average of 21 injections of mapharsen (dosages ranging from 2 to 40 mg.). Among these 45 patients 25, or 55.5 per cent, showed an improvement in their serologic reaction (complete reversal in 8 cases) after they had received 27.3 (average) mapharsen injections. In the remaining 20 cases, or 44.5 per cent, the serologic reaction remained unchanged after an average of 20 injections were given (table 1).

In all cases of late congenital syphilis the mapharsen therapy was supported by injections of bismuth compounds. Twenty-eight patients were treated with the alternate method of administration of bismuth compounds and mapharsen. In 17 cases the concurrent method of administration was used, and in most of these cases courses of bismuth and mapharsen administered concurrently were followed by separate courses of bismuth and mapharsen given alternately. There was a slight difference in the serologic results obtained in cases treated with these two methods, that is, in cases treated with the concurrent method the serologic improvement occurred in 58.5 per cent, while in cases treated by the alternate method a serologic improvement occurred in only 53.5 per cent (table 2).

TABLE 2.—*Influence of the Methods of Administration of Mapharsen and Bismuth on the Effectiveness of the Therapy in Late Congenital Syphilis*

	Total	Improved	Unimproved
A—Patients treated with the concurrent method	17	10 (58.8%)	7 (41.2%)
Patients treated with the alternate method only	28	15 (53.5%)	13 (46.5%)
		Concurrent Method Used in	
B—Improved cases	25	10 (40%)	
Unimproved cases	20	7 (35%)	

Among the improved cases the concurrent method was used in 40 per cent, while among the unimproved cases this method was used in only 35 per cent (table 2).

Four cases in which the serologic reaction remained unchanged when the alternate method was used showed a definite improvement when bismuth compounds and mapharsen were administered concurrently.

The effect on the serologic reaction was studied in the cases treated with the alternate method after an average of 19.1 injections of mapharsen and 29.7 injections of bismuth compounds had been given. The group treated with the concurrent method received an average of 22.5 injections of mapharsen and 23.6 injections of bismuth.

Effect of Mapharsen Therapy on the Serologic Reaction in Early Congenital Syphilis (tables 3 and 4).—Ten cases were studied. The dosage of mapharsen given was larger than the one used in the previous investigation.[8] The maximum dosage was 1 mg. per kilogram of weight. Because of the increased dosage of mapharsen, and in order to avoid possible toxic reactions, mapharsen and bismuth compounds were given in alternate courses in most cases. Treatment was usually begun with 1 to 2 mg. and increased weekly by 1 mg. until the maximum dosage was reached (1 mg. per kilogram of weight). The average dosage for the improved and unimproved cases was 6.5 mg. and 5.9 mg. respectively. In 1 case the maximum dosage was 15 mg. If we regard the improvement in case 1 as a very slight one and put it in the group of unimproved

TABLE 3.—*Effect of Mapharsen Therapy on the Serologic Reaction of Early Congenital Syphilis*

Name	Age	Number of Mapharsen Injections	Average Dosage of Mapharsen	Number of Bismuth Injections	Method of Administration of Mapharsen and Bismuth	Serologic Reaction	
						Before Treatment	After Treatment
G. C.	6 mos.	21	7.3	25	Alternate	4	3
W. J.	18 mos.	3	1.7	9	Alternate	4	1
J. H.	24 mos.	39	8.8	40	Alternate	4	Negative
C. J.	9 mos.	12	4.2	8	Alternate	2	2
C. G.	22 mos.	18	5.4	20	Concurrent	4	Negative
G. W.	1½ mos.	9	2.0	4	Concurrent	4	Negative
G. J.	2 mos.	10	4.0	17	Alternate	4	2
K. J.	24 mos.	30	7.9	20	Alternate	4	1
H. G.	6 mos.	10	5.1	14	Alternate	4	4
S.	1 mo.	12	3.7	3	Alternate	4	2

7. Levin, E. A., and Keddie, Frances: Toxic Effects Following the Use of Mapharsen, J. A. M. A. **118**: 368 (Jan. 31) 1942.
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10. Howles, J. K.: The Treatment of Congenital Syphilis with an Intravenous Arsenical, South. M. J. **32**: 940 (Sept.) 1939.
11. Wile, U. J.: In discussion on Foerster and others.[2]

cases, we may say that 7 out of 10 cases, or 70 per cent, showed a partial or complete reversal of the serologic reaction following the injection of 17.3 mg. (average) of mapharsen. (The serologic reaction reversed to negative in 3 cases, table 4.) It is also of significance that in both cases in which the concurrent method of administration of bismuth compounds and mapharsen was used the serologic reaction reversed to negative after an average of 13.5 injections of mapharsen were given.

Spinal Fluid Findings.—The spinal fluid was studied in 40 cases. The results of the examinations were negative except in 2 cases. In 1 case (M. G.), of frequent convulsions, with some change in the colloidal gold curve (1232210000) in an otherwise negative spinal fluid there seemed to be improvement under the influence of mapharsen therapy.

Patient 2 (baby S.), whose mother had syphilis, was apparently normal at birth but on the second day of life began to develop respiratory and feeding difficulties and was put under a constant oxygen tent. Because of the positive cord Wassermann test and x-ray findings of the long bones (syphilitic periostitis) it was thought that the broncholaryngeal collapse might be due to congenital syphilis. Antisyphilitic therapy was instituted. Three injections of a bismuth compound were given followed by twelve injections of mapharsen, starting with a dosage of 0.5 mg. and increasing each time by 1 mg. until 5 mg. was reached. After four months of therapy the spinal fluid, which was strongly positive for syphilis, became completely negative. The Wassermann reaction of the blood was 2 plus. The baby gained 6 pounds (2.7 Kg.), became more active and was not listless. However, the patient presented a pronounced hydrocephalus [12] (ventriculographic study of the skull revealed a tremendous dilatation of both ventricles) which increased in size somewhat in spite of antisyphilitic therapy.

TABLE 4 *(Analysis of Table 3).—Effect of Mapharsen Therapy on the Serologic Reaction of Early Congenital Syphilis*

1. Number of cases in which the serologic reaction was studied	10
2. Number of cases in which the serologic reaction reversed partly or completely	7 (70%)
3. Number of cases in which the serologic reaction did not change	3 (30%)
4. Average number of mapharsen injections in improved cases	17.3
5. Average dosage of mapharsen in improved cases	6.5 mg.
6. Average number of mapharsen injections in unimproved cases	14.3
7. Average dosage of mapharsen in unimproved cases	5.9 mg.

Effect of Mapharsen Therapy in Cases of Interstitial Keratitis.—Five patients were observed and they seemed to have benefited greatly by mapharsen therapy. In 1 case, in which the condition gradually became worse while sulfarsphenamine injections [12] were being given, there was a decided improvement in the cornea and in vision following ten injections of mapharsen. The second case cleared up almost entirely after five mapharsen and ten bismuth injections were given concurrently. The third patient was readmitted to the Metropolitan Hospital several times because of a recurrent interstitial keratitis. The Wassermann test was persistently negative but the interstitial keratitis improved each time mapharsen therapy was given concurrently with a bismuth compound. The fourth patient also showed a definite improvement following the alternate administration of mapharsen and bismuth courses. The fifth patient (W. G.) was admitted to the Metropolitan Hospital with the history of progressive blindness for two months. Concurrent administration of mapharsen and a bismuth compound was instituted and the patient showed improvement after four weeks of therapy. Later on, potassium iodide and boiled milk injections were added to the therapy. The interstitial keratitis was arrested and improved. The serologic reaction, however, did not change following thirty-six mapharsen and thirty-seven bismuth injections.

Congenital Syphilis and Pregnancy.—Six patients were observed; one of them is now in the fifth month of pregnancy and is receiving weekly injections of mapharsen without any untoward reactions. Five patients gave birth to normal, nonsyphilitic children after having received throughout pregnancy an average of 12 injections of mapharsen and 13 injections of a bismuth compound given in alternate courses. Both the cord and the blood Wassermann reactions were negative in 4 cases. In the fifth case only the cold serologic test was taken and this was found to be negative. All 6 patients tolerated the injections of mapharsen well and had no untoward reactions with the exception of 1 patient, who developed nausea once, and another who developed pruritus. In 2 cases the injections of mapharsen were accompanied by injections of liver extract without any ill effects on the patients or the course of their pregnancies.[13]

Untoward Reactions.[14]—The majority of our patients tolerated the injections of mapharsen well and showed no untoward reactions. Among 68 patients with congenital syphilis who received altogether 1,507 injections (1,012 intravenously and 495 intramuscularly) there were 15 who developed some kind of reaction. Altogether 17 reactions were observed. Of these, 9 were of a mild character and presented some mild gastrointestinal disturbance such as nausea, vomiting or fever. These reactions occurred generally only once and did not recur after the dosage of mapharsen was diminished. There were 7 delayed reactions in 7 patients. Three developed pruritus. In 2 cases the pruritus did not recur when prophylactic liver extract injections were given.[13] In the third case the pruritus was not prevented nor alleviated by concurrent liver extract injections [13] and mapharsen had to be discontinued. Two patients developed erythematous eruptions lasting for a few days. One patient (A. H., a boy aged 11 years, weight 83 pounds, 37.6 Kg.) developed jaundice following 10 mapharsen injections (7.5 to 25 mg.), which were given concurrently with bismuth; one patient developed a moderate anemia combined with poikilocytosis and anisocytosis.

The ratio of immediate reactions to the general number of injections was 9:1,501 or 1:167.4. The ratio of delayed reactions to the general number of injections given was 1:214.4. These data contain a higher percentage of untoward reactions than our previous investigation [8] in cases of congenital syphilis, in which the respective ratios were 1:883 and 1:441. The higher frequency in immediate and delayed reactions in our

12. The baby died on June 7. Autopsy revealed lung abscess and hydrocephalus as causes of death. Examination of all viscera showed no evidence of damage due to medication (Saccone, Andrea: Personal communication to the authors).

13. Astrachan, G. D., and Sharp, E. A.: The Value of Administration of Liver in Patients Intolerant to Arsenicals, J. Invest. Dermat. 1: 427 (Dec.) 1938. MacKee and Astrachan.[37]

14. Local complications and pain after injection will be discussed elsewhere.

present series could be explained by the use of the intramuscular method of administration of mapharsen in many cases (pain may often be followed by nausea and vomiting) and by the increased dosage of mapharsen from 0.5 mg. to 1 mg. per kilogram of weight. Even these figures are lower than in our previous paper, which dealt chiefly with adult patients.[15] In this group the respective ratios were 1:60.4 and 1:121. This proves that mapharsen is less toxic to children than to adults. Nine (0.06 per cent) immediate gastrointestinal reactions were observed in 1,507 injections. This incidence is small in comparison with that of the arsphenamines, following which there have been, according to various observers, from 7 to 25 per cent[16] of mild reactions.

The lower index of toxicity of mapharsen is also illustrated by the following: Three of our cases suffered from severe gastrointestinal disturbances (vomiting, headache) after the injections of neoarsphenamine. These patients tolerated mapharsen well. No reactions developed. One patient had a generalized erythema, a scaly eruption following an injection of 0.2 Gm. of arsphenamine. The patient received, one and one-half years later, a course of 14 mapharsen injections (dosage 5 to 35 mg.) without any after-effects. On the other hand, only 1 patient sensitive to mapharsen (developed urticaria) tolerated neoarsphenamine well.

Blood Count Examinations.—Blood count studies were done in 48 cases. In most of the cases the blood count did not show any changes following mapharsen therapy. However, in 5 cases a decrease in the red blood cell count was noted (average decrease 620,000) as well as a lowering of the hemoglobin (average decrease 14 per cent) following 8.4 (average) of mapharsen injections. In 1 of these cases (G. H., aged 6 months) following 8 injections of mapharsen (average dosage 5.1 mg.) the aforementioned changes in the red blood cell count and hemoglobin appeared together with poikilocytosis and anisocytosis. Three among these 5 patients were infants who tolerated the injections of mapharsen well and did not show any signs of discomfort or illness. The changes in the blood counts were discovered by routine repeated blood examinations. These changes in the blood counts were not of a grave character; however, they occurred in 3 of 10 cases of early congenital syphilis. And in our opinion that is quite a high percentage. This could be coincidental, but it could also quite possibly be explained by the high dosage of mapharsen given in the early cases (maximum dosage 1 mg. per kilogram of weight).

Liver Function Tests.—Icterus indexes were performed in 32 cases. The majority of the tests were found to be normal. Following mapharsen therapy the icterus indexes were found to be elevated in 5 cases. In 3 of these cases (3 of 32, or 9.4 per cent) the icterus indexes were 10 to 12, in the other 2 (2 of 32, or 6.3 per cent) the indexes were 8 to 9.3. These percentages of 9.4 and 6.3 compare favorably with the figures on changes in the icterus indexes in one group of adults treated with mapharsen, in which the respective percentages were 19 and 19.[17] This fact proves again that mapharsen is less toxic in children than in adults. It is also noteworthy that 2 out of 3 patients with icterus indexes of 10 to 12 were children treated by the concurrent method of administration of mapharsen and bismuth. In 2 cases the icterus indexes were found to be somewhat elevated (8.3-10) before mapharsen therapy was instituted. Mapharsen was then administered accompanied each time by an injection of liver extract.[18] Following ten mapharsen injections and ten liver injections the icterus indexes in both cases became normal.[17]

Local Complications[18] (tables 5 and 6).—In a previous paper[8] the fact was mentioned that the patients with early congenital syphilis[19] who received the injections of mapharsen intramuscularly did not show any signs of general discomfort (fever or restlessness) or any local reaction (necrosis on the site of the injection). We may say that our present investigation confirmed these findings. We had the same experience with all our cases of early congenital syphilis with the exception of 1 case in which crying and restlessness occurred for the entire day following the injection of 8 mg. of mapharsen. The patients with early congenital syphilis received altogether 138 intramuscular injections, and the maximum dosage administered was 15 mg.

TABLE 5.—*After-Effects of the Intramuscular Administration of Mapharsen in Adults*

Total number of patients treated	19
Total number of injections given	235
Number of injections which were followed by very mild soreness (duration ¼-1 hour)	129
Number of injections which were followed by slight or moderate pains (duration 1-6 hours)	54
Number of injections which were followed by severe pain (duration 6-24 hours)	46
Number of injections which were followed by long lasting severe pains (duration 2-10 days)	6

Since it is very difficult to evaluate the kind and amount of pain in infants, we decided to use the intramuscular method for children old enough to be interrogated about the after-effects. Nineteen children from 3 to 12 years of age with late congenital syphilis were treated. The maximum dosage in many of these cases was as high as 20 mg.; 357 injections were given. The information about the pain was obtained from the children, the parents or the ward nurse in charge.[20]

All children, with the exception of those who had special complaints, stated that the injection of mapharsen was followed by a mild soreness lasting from a quarter of an hour to one hour. Special complaints were recorded by 9 patients after 60 injections. Forty-five of these complaints were of slight or moderate pain lasting from one to four hours. These pains did not interfere with the children's usual activities, such as playing and walking. Fifteen other complaints were of severe pain sometimes lasting almost an entire day. In 1 case the pain, after an injection of 2 mg., lasted all night and was accompanied with vomiting. The patient also vomited the entire week following an injection of 4 mg. of mapharsen. The same patient later received 5 more injections of mapharsen (dosage 4 to 12 mg.)

15. Astrachan, G. D.: Mapharsen in Antisyphilitic Therapy, Am. J. Syph., Gonor. & Ven. Dis. **21**: 81 (Jan.) 1937.
16. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C Thomas, Publisher, 1941.
17. MacKee, G. M., and Astrachan, G. D.: The Value of Liver Extract in Cases Intolerant to Arsenicals, Heavy Metals and Radiation, J. Invest. Dermat. **3**: 409 (Oct.) 1940.
18. Mapharsen was dissolved in isotonic solution of sodium chloride, 60 mg. to 10 cc. of solution (Sharp, E.: Personal communication to the authors). Later a more concentrated solution was used (60 mg. of mapharsen to 5 cc. of saline solution). For the last three months plain distilled water has also been used as a solvent. Our impression is that the concentration of mapharsen and the kind of solvent used have little if any influence on the amount and kind of complications.
19. The use of mapharsen in early congenital syphilis was suggested by Dr. Rosen (cited by Astrachan[15]).
20. Ramsden, F.: Personal communication to the authors.

without any special complaints. In another case the pain lasted for about twenty-four hours several times, and the intramuscular method of administration of mapharsen in this case was abandoned.

The Intramuscular Use of Mapharsen for Adult Patients (table 5).—Children are prone to forget pain on its cessation; they may even discount it or overlook it in the heat of an interesting or competitive game. It is questionable, therefore, whether the answers given by children can be used for evaluation of the kind and degree of after-effects following the intramuscular administration of any medication. It is for this reason that we decided to include in this investigation information about local complications following the intramuscular use of mapharsen to adult patients. They were selected mostly from among obese women in whom intravenous therapy was impossible because of bad veins. Nineteen cases were observed and 235 injections were given. The maximum dosage administered was 30 mg. and the number of injections given varied from 1 to 36. The initial dosage was 4 mg. It was increased weekly by 2 mg. until 30 mg. was reached. The very gradual and slow increase in the dosage can easily be understood if it will be remembered that in experiments of this kind one must proceed with caution because of the possibility of serious complications.

The patients were interrogated each time as to the presence or absence of any reactions, the kind and degree of pain, if any, following the injections of mapharsen. As with the children, all patients, with the exception of those who had special complaints, stated that the injection of mapharsen was followed by a mild soreness lasting from a quarter of an hour to one hour. Special complaints were recorded after 106 injections were given to 17 patients; 54 of these complaints were of slight or moderate pain lasting generally from one to six hours. One patient complained once of a sensation which felt as if "some one was drilling the bone," and the pain lasted all day. The same patient, however, stated that she had no pain at all after the succeeding injection of mapharsen. One patient complained of a slight pain lasting for two days; another of the same group stated that the pain was less pronounced than that experienced after bismarsen injections. Prior to the institution of mapharsen therapy 1 patient was treated with intramuscular injections of sulfur arsphenamine (0.1 to 0.2 Gm.). She stated that after each injection she suffered a severe burning sensation which lasted for several hours, while the injections of mapharsen did not cause any after-effects. The other fifty-two special complaints were of pains which could be classified as severe. These lasted in the average for six to twenty-four hours and even longer. These pains were characterized as "shooting" or "sharp" or the patient complained of inability to walk or severe pain in the leg causing incapacitation for three days. Three patients complained of pain lasting about a week. One complained of pain lasting ten days. It is interesting to note that some of these patients, after complaining of severe pain several times, stated that the pain was very slight at the next visit, even though the dosage of mapharsen was the same or even larger.

COMMENT

This investigation confirmed our conclusions in previous investigations that mapharsen is a useful drug in the treatment of cases of late congenital syphilis.[21] In 55.5 per cent of our cases the blood serologic reaction reversed partially or completely. This percentage is a fairly good one in cases of late congenital syphilis, in which in not less than 50 per cent of instances there is a fixed serologic reaction, regardless of treatment given.[22] The fact that improvement occurred in all 6 cases of interstitial keratitis following mapharsen therapy emphasizes its value in cases of late congenital syphilis.

In a previous contribution a preference was expressed for the concurrent method of administration of bismuth compounds and mapharsen when dealing with cases of late congenital syphilis.[15] With regard to this problem an analysis of the serologic response in our cases showed that there were more improved cases (58.8 per cent) among those treated with the concurrent method than among those treated with the alternate method (53.5 per cent). The concurrent method was used more among the improved cases (40 per cent) than among the unimproved ones (35 per cent). Although the difference in percentages is a very small one, it still points to a favorable influence of the concurrent method on the effectiveness of mapharsen therapy. (The influence of the slightly higher number of injections of mapharsen given in the concurrent group over that given in the alternate group may be discounted because the average number of bismuth injections given in the alternate group was larger than that given in the concurrent group.

Four of our cases showed an improvement only when the concurrent method was used; this also points to the advisability of the use of this method. On the other hand we have to admit that the concurrent method is more liable to cause untoward reactions than the alternate one (case A. H., jaundice). For this reason the concurrent method should be used only for healthy patients and it should be combined with the alternate method of administration, that is, a course of bismuth and mapharsen given concurrently should be followed by courses of bismuth and mapharsen given alternately. It is also imperative that the patients be carefully observed and frequent blood counts and liver function tests be done.

In 7 out of 10 cases of early congenital syphilis the serologic reaction reversed partly or completely after an average of 17.3 injections of mapharsen were administered. A positive spinal fluid in a 4 months old baby reversed to negative after 3 bismuth and 12 mapharsen injections were administered. These data confirm our opinion in our previous investigation [8] that mapharsen may be useful in cases of early congenital syphilis. Further observation of the efficacy of this drug in many more cases will be necessary before we can come to a definite conclusion.

Because of the large number (3 out of 10 cases) of early congenital syphilis in which regressive changes in the blood count could be attributed to mapharsen therapy, we feel that the maximum dosage employed by us (1 mg. per kilogram of weight) was probably too high for infants, who are usually in a weakened condition as the result of their lowered resistance, malnutrition and toxemia, which are caused by the spirochetosis. On the other hand, the maximum dosage employed in our previous investigation [8] (0.5 mg. per kilogram of weight) did not cause any after-effects.

21. Astrachan.[15] Cornell and Astrachan.[8]

22. Cole, H. N.; Usilton, Lida J.; Moore, J. E.; O'Leary, P. A.; Stokes, J. H.; Wile, U. J.; Parran, Thomas, Jr., and Vonderlehr, R. A.: Late Prenatal Syphilis, with Special Reference to Interstitial Keratitis: Its Prevention and Treatment, Arch. Dermat. & Syph. **35**: 563 (April) 1937. Moore.[16]

We feel, therefore, that 0.75 mg. per kilogram of weight would be the optimum dosage for cases of early congenital syphilis.

The maximum dosage of mapharsen in some of our cases of late congenital syphilis was somewhat higher than in the first investigation [8] (0.75 to 1 mg. instead of 0.5 mg. per kilogram of weight). In view of the relative increase in the ratio of reactions in this series, we believe that 0.75 mg. per kilogram of weight would probably be the most suitable dosage in cases of late congenital syphilis.

As to the question of the lower toxicity of mapharsen in comparison with other arsenicals, we stress the absence of exfoliative dermatitis, nitritoid reactions, the small number of immediate and delayed reactions in our series and the fact that several of our patients who were sensitive to neoarsphenamine tolerated mapharsen well. The lower ratios of reactions in our series in comparison with those in a previous paper [15] which dealt chiefly with adult patients proves again that mapharsen is less toxic in children than in adults. This is also confirmed by the very small percentage of increased icterus indexes in comparison with that of the adult group.[17]

It is also noteworthy that all 6 pregnant women tolerated mapharsen well and developed no untoward reactions, except 1 case of nausea (once) and 1 of pruritus. This seems to confirm the opinion of one of us about the low toxicity of mapharsen in cases of syphilis and pregnancy.[23]

Where the question of the feasibility of intramuscular administration of mapharsen is concerned, we stress the facts that, while some patients complained of severe and long lasting pain, the majority of the injections (in adults) were followed by slight or moderate pain only, that not a single case of local necrosis developed following 730 intramuscular injections of mapharsen (in adults and children) and that serious systemic complications did not appear as a result of this method of administration.

It is also noteworthy that 2 patients who received sulfarsphenamine or bismarsen therapy prior to mapharsen injections stated that the intramuscular injections of mapharsen caused less pain and discomfort than the two aforementioned drugs. Taking all this into consideration, we feel justified in stating that in selected cases the intramuscular method of administration of mapharsen may be tried. It should be employed, however, very cautiously, the dosages increased very slowly, and only those cases treated in which all attempts at intravenous therapy have failed.

CONCLUSIONS

1. Mapharsen is a good drug for patients with late congenital syphilis.

2. It is useful in cases of interstitial keratitis.

3. The concurrent method of administration of bismuth compounds and mapharsen in late congenital syphilis should be used for healthy patients only and should be combined with the alternate method of administration. Frequent blood counts and liver function tests should be performed on these patients.

4. Mapharsen proved to be useful in our cases of early congenital syphilis.

5. Further observation of many more cases will be necessary in order to come to a definite conclusion about the efficacy of mapharsen in early congenital syphilis.

6. We believe that 0.75 mg. per kilogram of weight should be the maximum dosage for patients with any form of congenital syphilis.

7. Mapharsen is less toxic to children than to adults.

8. Mapharsen can be given intramuscularly in selected cases; however, it should be used only in cases in which all attempts at intravenous therapy have failed.

9. Further experimentation with various solvents is desirable in order to find the least painful method of intramuscular administration of mapharsen.

23. Astrachan, G. B.: Syphilis in Pregnancy, New York State J. Med. **40**: 43 (Jan. 1) 1940.

ABSTRACT OF DISCUSSION

DR. NORMAN R. INGRAHAM JR., Philadelphia: Many of the studies of a few years ago having to do with the treatment of congenital syphilis (particularly of early congenital syphilis) have had their present scientific value greatly diminished because of a lack of appreciation of the conditions affecting the interpretation of the blood serologic test for syphilis in infancy, because of the roentgenogram in the first few months of life or through a failure on the part of the various authors to make clear the diagnostic standards employed. Moreover, the inability to keep these patients under treatment observation with sufficient regularity for a long enough period of time to make available mass statistics has rendered information concerning the long time results of treatment of congenital syphilis hard to obtain. Information such as has been presented could be rendered even more valuable by the addition of brief statements concerning (1) the diagnostic criteria employed, (2) the dosage interval and the regularity of administration of treatment and (3) the total duration of observation. These suggestions would apply to the medical follow-up of the apparently normal infant offspring of the six syphilitic mothers included in the study as well as to the proved cases of congenital syphilis. I have had no personal experience with the use of intramuscular mapharsen in the treatment of congenital syphilis. The intramuscular arsenicals which I have used routinely for infants over a period of years, namely sulfarsphenamine at the Philadelphia General Hospital and bismarsen at the University Hospital, have been therapeutically effective and have resulted in no serious problems from the standpoint of either local or systemic reaction. In the dosage that is used for small infants, even neoarsphenamine may be given intramuscularly (or under the fascia of the scalp). Intramuscular arsenical therapy has definite indications in the treatment of infantile congenital syphilis and in some stages of adult syphilis. I feel, therefore, that this evidence of the possible value of intramuscular mapharsen in the treatment of congenital syphilis is particularly timely.

DR. JOHN E. RAUSCHKOLB, Cleveland: In general my observations agree with those of the authors; that is, mapharsen is not only a good but an excellent drug in the treatment of congenital syphilis, especially the early types, for it is in this stage that the arsenicals are of the most value in preventing the destructive changes. The dosage I use is even more conservative, it being 0.5 mg. per kilogram of body weight as a maximum. Mapharsen can be given intramuscularly with safety. Especially is this true in the early congenital types. The drug should be given in concentrations of 10 per cent strength in order to keep down the volume, thus minimizing inflammatory areas at the site of the injection. Needless to say, these injections should be given in the upper outer quadrant of the buttocks and intramuscularly; otherwise, abscess may follow. I have had one abscess develop, in which concurrent therapy was administered, consisting of both mapharsen and bismuth salicylate injections. Of course, this complication may have been produced by bismuth or a combination of bismuth and mapharsen. In my experience solvents play but a minor factor in preventing pain, but the solvent may raise the incidence of toxic reaction. I now am using only distilled water in concentrations of 5 to 10 per cent. I cannot agree with the authors as to its usefulness in interstitial keratitis. In my experience mapharsen had no beneficial results on this late acute congenital manifestation. Perhaps their improvement may be the combined effect

of foreign protein reaction produced by the drug given intramuscularly plus the drug action.

DR. GIRSCH D. ASTRACHAN, New York: Follow-up of cases is important; this was attempted by the social service department and in some cases useful information was obtained, but there are difficulties. The proper procedure in intramuscular therapy is for the injections to be administered by one individual all the time. All the intramuscular injections given in the Metropolitan Hospital Dispensary were administered by one man only (Dr. Israel Hirshon). In our previous investigation the dosage used was 0.5 mg. per kilogram of body weight. This dosage was found somewhat ineffective and we decided to increase it. We now feel that 0.75 mg. per kilogram of body weight would be the proper dosage. The concurrent method was avoided in most of the cases of early congenital syphilis because of the increased dosage of mapharsen employed and also because we felt that infants who are usually in a weakened condition as a result of their lowered resistance, malnutrition and toxemia may develop reactions if the concurrent method is used. These patients were treated continuously by alternate courses of bismuth and mapharsen. Among our cases were 3 of an acute form of interstitial keratitis, and all these responded well to mapharsen therapy.

Clinical Notes, Suggestions and New Instruments

A DEVICE FOR DETECTING SIMULATED UNILATERAL DEAFNESS

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Simulated unilateral deafness is sometimes practiced in wartime among draftees in order to avoid military conscription and among soldiers to avoid duty or to claim compensation after military discharge.

Most cases of suspected simulated deafness are unilateral. This is due to the fact that a double deafness would previously have attracted attention, whereas a onesided deafness might have existed without being detected. Also it is easier to simulate onesided deafness.

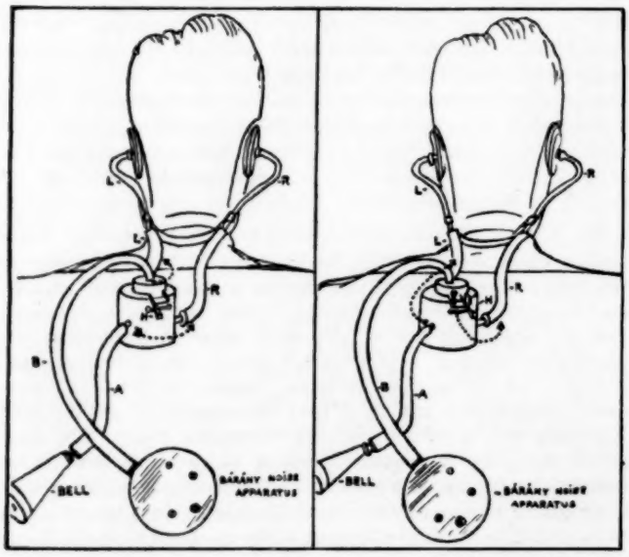

Fig. 1.—Left: Words spoken into bell *A* will be conveyed into suspect's right ear only, and the noise from the Bárány apparatus will enter the left ear. Right: The procedure is reversed. Now the spoken words enter the suspect's left ear, and the noise his right ear.

The examiner must keep in mind that many of these persons have given considerable study to the malingering tests and have developed shrewd technics in carrying out their attempts to deceive. After some practice the malingerer has learned to ignore sounds, tones and words directed toward the ear in which he is simulating deafness. He also learns when to elevate the pitch of his voice during the examination.

The tests now in use, while attaining a certain degree of success, are not foolproof. The tests widely used are:

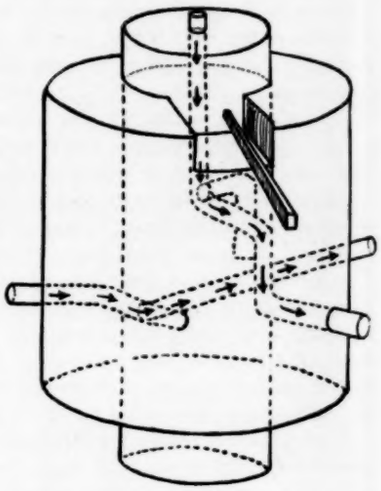

Fig. 2.—The inner workings of the two in one petcock.

1 *Stethoscope Test.*—A common stethoscope, having one tube closed with a wooden plug, is adjusted to the patient's ears, the open tube to the suspected ear and the closed one to the normal ear. The examiner speaks into the bell of the stethoscope, having the patient repeat what he hears. The stethoscope is then removed, the normal ear is tightly closed and the same formula is repeated to the patient. He will say he cannot hear, whereas he has already repeated after the examiner with the normal ear tightly closed with the plugged arm of the stethoscope.

This test is frequently unsuccessful if the malingerer has learned to ignore all sounds going to the suspected ear.

2. *Lombard's Test.*—The patient reads some selected passage aloud. As long as he hears his own voice it does not change in pitch or articulation. The Bárány noise apparatus is then applied to the sound ear while he continues reading. If he is actually deaf in the other ear, his voice will become elevated in pitch and his articulation blurred. If he hears with that ear, his voice will remain unaffected.

This test can also fail in its purpose if the patient learns to elevate his voice when the noise apparatus is directed to his normal ear.

3. *Double Conversation Test.*—This test is done by two examiners. Simultaneously each examiner tries to hold a conversation with the suspect through a tube leading to each ear. In unilateral deafness the suspect will ignore the conversation directed to the affected ear. However, a good malingerer with a little practice can learn to ignore the conversation directed toward the ear in which he is simulating deafness.

All other tests for unilateral deafness are variations of the same principles.

MODE OF OPERATION OF AUTHOR'S TEST

The device described in this paper makes use of these tests in a new way. By interfering with the malingerer's powers of concentration, it renders him helpless to carry out his purpose.

A common stethoscope is adjusted to the suspect's ears with the bell behind his back. At the fork of the stethoscope is set a two in one petcock (fig. 1) fitted with tubes *A* and *B*. The stethoscope bell is attached to the far end of tube *A*, the Bárány noise apparatus to the far end of tube *B*. When the handle of the petcock (fig. 1, left) is moved clockwise until blocked, words spoken into the bell will be conveyed to the suspect's right ear only and the noise from the Bárány apparatus will enter his left ear. The procedure is then immediately reversed by moving handle *H* counterclockwise (fig. 1, right). Now the spoken words enter the suspect's left ear, and the noise his right ear. The result is that the subject is bewildered, as shown by his responses to the standard tests.

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1. *Stethoscope Test.*—In true unilateral deafness, the normal ear will perceive the spoken voice or alternating noise, and the subject will respond promptly. The malingerer hears the noise and the spoken voice simultaneously but cannot tell to which ear each is directed. A turn of the handle, interchanging the direction of the spoken voice and noise, will increase his indecision. He will not be able to respond properly.

2. *Lombard's Test.*—In true unilateral deafness the patient reading aloud will automatically raise his voice when noise is directed to the normal ear and lower it when the noise is switched to the other ear. But the rapid shift of the noise from one ear to the other by my instrument confuses the malingerer. He will not be able to synchronize his tone with the rise and fall of the noise.

3. *Double Conversation Test.*—The Bárány noise apparatus is replaced by a second stethoscope bell. Simultaneous conversations carried on by two examiners will not confuse a genuine unilateral deaf person, for he can perceive only one voice. The malingerer, however, will hear both voices, and their rapid changing from one ear to the other will greatly confuse him and prevent him from making proper responses.

RESULTS OF TESTS

This device has been put to actual use at the Station Hospital, where it was developed by the author, while Lieut. Col. Carl A. Schuck was commanding officer. It has been found to be very valuable in detecting simulated unilateral deafness. Even if the malingerer knows of the tests he cannot protect himself against them; he gives himself away. The device therefore seems to offer a foolproof application of the accepted means of examining this type of case.

A SIMPLE HOLDER FOR THE ADMINISTRATION OF PENTOTHAL SODIUM

CAPTAIN ROBERT B. HOPE
MEDICAL CORPS, ARMY OF THE UNITED STATES

Intravenous anesthesia has reached an established place in the armamentarium of the civilian anesthetist. It is now coming to the foreground more and more in the practice of military medicine. It is adaptable in selected cases to surgery both in the field and in the hospital. The anesthetic of choice is pentothal sodium. When judiciously used by a trained anesthetist, anesthetic complications are very few.

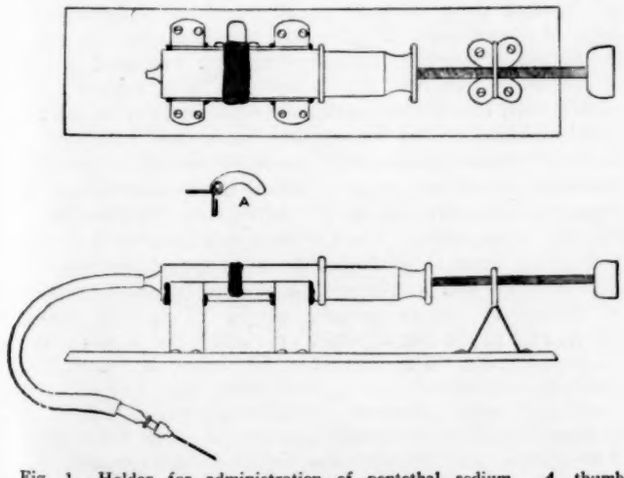

Fig. 1.—Holder for administration of pentothal sodium. *A*, thumb catch which holds 50 cc. syringe in cradle.

Pentothal sodium is best given in a 2.5 per cent solution. Dilution to this strength necessitates using a large syringe. It is important that during the administration of pentothal sodium a free airway be maintained at all times, which is accomplished by continuously holding up the patient's jaw. To do this, hold a needle attached to a large syringe in place. It is impossible for the anesthetist to administer the anesthetic as well as oxygen if necessary, unless he has an assistant. This has been obviated by the development of a mechanical holder for the pentothal syringe. These are made somewhat on the principle of the mechanical stage, so that the anesthetist can merely turn a thumb screw and administer the anesthetic. There are several models manufactured; they are relatively expensive and sometimes not readily obtainable, especially overseas. Not one was available to me.

Fig. 2.—Apparatus in use in operation: open reduction of clavicle.

I presented the problem to our utilities department. The principle and the general needs the instrument must meet were described. For the mechanical part, to push the plunger home a 4½ inch long, ¼ inch diameter bolt and nut were used. The instrument was made to accommodate a 30 cc. syringe, since we had more of that size on hand than the 50 cc. size. The latter size would probably be preferable.

The instrument depicted in figure 1 was the result. It is simple, entirely dependable and satisfactory in operation. The cost of making is but a few hours time. The materials can be found in any utilities department: a bolt and nut, some light weight sheet metal, some inner tube rubber, a cap from a metal cot post and some screws. It is an example of the ingenuity and resourcefulness that we continually find in the utilities departments of our various units. We feel that we are particularly fortunate to have such personnel in our organization.

USE OF THE INSTRUMENT

The setup is very simple. A 30 cc. syringe will accommodate the 40 cc. of solution that is necessary in diluting 1 Gm. of pentothal to make a 2.5 per cent solution. The full syringe is placed in the holder. A latex rubber tube 20 cm. in length with a ground glass adapter and 20 gage needle is attached to the syringe. The pentothal solution is then forced out to the needle, and the tube is filled by pushing the plunger home. This brings the solution to about the 30 cc. mark in the syringe. The needle is inserted in the vein in the usual manner. Pentothal can then be administered at will by merely turning the thumb screw.

In surgery a number of syringes, needles and units of rubber tubing with adapters are kept in separate sterile packs. With ordinary sterile technic, by merely changing the tubing unit and needle, pentothal sodium solution left in the syringe is still sterile and usable for another case. Thus several short cases to be done in succession can be handled on one syringeful. If more pentothal is needed for the same case, the solution is mixed up in a new syringe and attached to the tubing and needle, which is still inserted in the vein.

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SEVERE RENAL IRRITATION RESULTING FROM FOREIGN PROTEIN (TYPHOID) FEVER THERAPY

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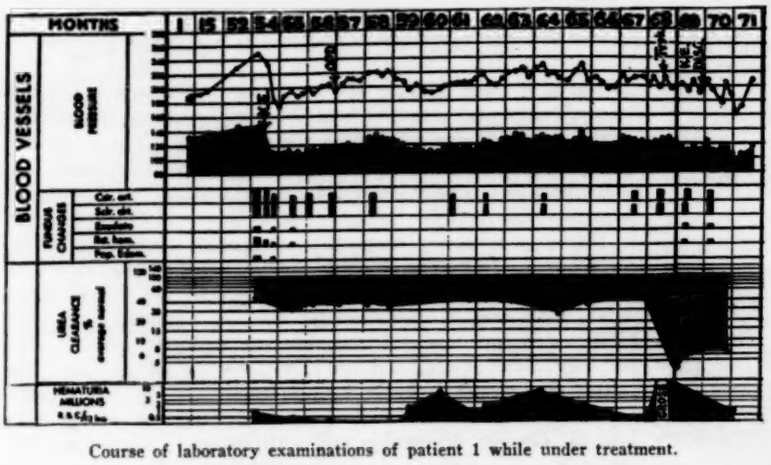
INDIANAPOLIS

We have recently studied 2 patients with renal disease in whom signs of severe renal irritation developed following fever induced by intravenous typhoid vaccine. Engman and McGarry [1] briefly describe a patient who developed microscopic hematuria after receiving intravenous typhoid vaccine, and Campbell [2] reported hematuria in an arthritic patient being treated with "nonspecific" protein (typhoid) fever therapy. In 1932 Hench [3] reviewed the usual and unusual reactions of typhoid vaccine protein therapy in a series of 2,500 patients. There were 14 unusual reactions in this series, 2 of whom died with anuria. At necropsy acute diffuse nephritis was found in 1 case and no renal lesion in the other. Our 2 patients had previous renal disease—the nephrotic stage of hemorrhagic Bright's disease in 1, and malignant hypertension in the other—conditions which might be contraindications to foreign protein therapy.[4]

Because pyrexia induced by injection of foreign protein has been suggested in the treatment of various types of vascular diseases, including hypertension, it has seemed to us well to point out by these 2 examples that it is a therapy not without danger, especially in those with preexisting renal damage.



Course of laboratory examinations of patient 1 while under treatment.

REPORT OF CASES

CASE 1.—A Negro woman aged 35 admitted to the Lilly Clinic complained of hypertension of two year's duration, headache, nausea and vomiting. She was bedridden for two months before admission. The arterial blood pressure was 240 systolic and 140 diastolic. Grade 4 constriction and sclerosis of the retinal arterioles, grade 1 retinal exudates, grade 2 retinal hemorrhages and grade 1 papilledema led to the diagnosis of malignant hypertension. Urea clearance was 47 per cent of the average normal. The maximal ability to concentrate urine was 1.020. There were 900,000 red blood cells in the twelve hour specimen of urine. The patient excreted about 1 Gm. of protein daily. The electrocardiogram showed left axis deviation.

She was treated for fourteen months with antipressor renal extracts which resulted in lowering the arterial blood pressure to an average of 200 systolic, 110 diastolic and regression of retinopathy with disappearance of hemorrhages, exudates and papilledema. During these fourteen months she had hematuria varying from normal to 5,500,000 red blood cells in twelve hours.

On May 21, 1942 it was decided to determine whether or not fever induced with typhoid vaccine could mimic the results of antipressor renal extracts. She was given an intravenous infusion of 100 cc. of isotonic solution of sodium chloride that contained 0.20 cc. of typhoid mixed vaccine according to the method of Solomon and Somkin.[5] After a violent chill, the temperature and pulse rate rose to 104 F. and 140 respectively and the respirations to 37. The following day gross hematuria was noted, but despite this a similar dose of mixed vaccine was given, again followed by a chill and a rise in temperature to 103.4 F. The gross hematuria persisted for ten days. There was no oliguria, edema or increase in arterial pressure. Urea clearance fell to 3 per cent of average normal. Nausea and vomiting developed and persisted for six weeks. During this time nonprotein nitrogen ranged between 100 and 207 mg. per hundred cubic centimeters, hemorrhages and exudates reappeared in the ocular fundi and the hemoglobin level fell to 37 per cent of normal. On July 27 urea clearance had risen to 7 per cent of average normal. The Addis count of the urinary sediment showed 750,000 red blood cells in twelve hours; the maximum ability to concentrate urine was to 1.012, and the hemoglobin level had risen to 43 per cent of average normal. Nausea and vomiting no longer occurred. The prognosis is grave, and it is doubtful that she will return to her former state of health.

CASE 2.—A white boy aged 2½ years was admitted to the Indianapolis City Hospital on May 19, 1938. Six weeks before admission the child had a rash followed in three weeks by swelling of his eyes, and still later by anasarca. The mother reported oliguria and increasing irritability. The physical findings on admission were temperature 99.4 F.; arterial blood pressure 114 systolic and 70 diastolic; there were generalized edema, ascites and moist rales over the base of the left lung. The urine contained 1.5 per cent albumin, 10 to 20 hyaline casts per high power field, a few pus cells and occasional red cells. Urea clearance was 100 per cent of average normal. The red blood cell count was 4.10 millions, the white blood cell count 6,500 and the hemoglobin level 61.4 per cent of normal. Total plasma proteins were 4.7 Gm. per hundred cubic centimeters; albumin was 0.6 Gm. per hundred cubic centimeters. A diagnosis of the nephrotic stage of hemorrhagic Bright's disease was made. He was in the hospital six months, during which time treatment consisted of bed rest, a salt free, low sodium diet, a high protein, high vitamin diet, intravenous acacia, and potassium citrate and mercurial diuretics. This management maintained edema in the grade 1 stage for the first three hospital months. At the end of the fourth month edema again became grade 4 and blood pressure rose to an average of 138 systolic and 100 diastolic. At this time it was decided to use triple typhoid vaccine in an effort to increase renal blood flow, thereby hastening recovery. On September 20, four months after admission, he was given 0.4 cc. of typhoid H vaccine intramuscularly. Two days later he received 0.6 cc., neither of which produced a rise in temperature. Two weeks later 0.1 cc. and 0.2 cc. of typhoid H vaccine intravenously produced no fever. Three weeks later 0.25 cc. of vaccine intravenously produced a temperature rise to 101 F. On October 18 0.3 cc. of typhoid vaccine was given intravenously. Three days later 0.5 cc. was injected intravenously. The maximum temperature rise was to 100 F. On the following day he was given 0.2 cc. of triple typhoid vaccine intravenously. The temperature rose to 101 F. Three days later urea clearance fell to 28 per cent of normal and gross hematuria appeared. Urinary protein increased from an average of 2.5 Gm. in twenty-four hours to 6 Gm. in twenty-four hours. Hematuria

From the Lilly Laboratory for Clinical Research, Indianapolis City Hospital.

1. Engman, M. F., and McGarry, R. A.: Treatment of Certain Diseases of the Skin, J. A. M. A. **67**: 1741 (Dec. 9) 1916.
2. Campbell, D.: Nonspecific Therapy in Rheumatoid Arthritis, Glasgow M. J. **103**: 79 (Feb.) 1925.
3. Hench, P. S.: Usual and Unusual Reactions to Protein (Fever) Therapy, Arch. Int. Med. **49**: 1 (Jan.) 1932.
4. Cecil, R. L.: A Report on Forty Cases of Acute Arthritis Treated by the Intravenous Injection of Foreign Protein, Arch. Int. Med. **20**: 951 (Dec.) 1917; Nonspecific Protein Therapy, J. A. M. A. **105**: 1846 (Dec. 7) 1935.
5. Solomon, H. A., and Somkin, Eugene: An Improved Method of Obtaining Sustained Controlled Hyperpyrexia with Triple Typhoid Vaccine, Am. J. M. Sc. **203**: 736 (May) 1942.

persisted between 750,000 and 2,500,000 red blood cells in twelve hours, and urea clearance was depressed below 60 per cent of average normal for three months. At no time was there oliguria, increase of edema or rise in arterial blood pressure. At the end of this time hematuria disappeared and urea clearance returned to normal. The child subsequently recovered from nephritis as evidenced by absence of edema and proteinuria, normal ability to concentrate urine (1.027) and a normal urinary sediment count on May 28, 1942.

COMMENT

Intravenously injected typhoid vaccine was used for these 2 patients in the hope that in the one suffering from malignant hypertension the fever induced would lower arterial pressure and in the other, with the nephrotic syndrome, that edema would disappear. Whatever therapeutic effect occurred was obscured by the appearance of signs of severe renal damage. The nature of the damage is not known, but that it was severe is indicated by diminution of urea clearance, azotemia and hematuria.

Typhoid vaccine has been widely used to induce fever in a variety of diseases and especially in arthritis and peripheral vascular disease. In most cases of this type renal disease is not present. Our experience suggests that preexisting renal disease should warn the clinician of the possible danger of this type of therapy.

CONCLUSIONS

Fever induced by intravenous injection of typhoid vaccine caused evidence of severe renal irritation in a patient suffering from malignant hypertension and in a patient in the nephrotic stage of hemorrhagic Bright's disease. It appears that patients with renal disease should be treated by this method with great caution if at all.

Special Article

STANDARDS OF EFFECTIVE ADMINISTRATION OF INHALATIONAL THERAPY

BY THE COMMITTEE ON PUBLIC HEALTH RELATIONS OF THE NEW YORK ACADEMY OF MEDICINE

The importance of inhalational therapy in modern medical practice is shown by its use in cardiac failure, coronary artery disease, asthma, atelectasis of the lungs of the newborn, postoperative atelectasis, pneumonia, pulmonary edema, emphysema and cerebral thrombosis. A proper understanding of the technic is especially necessary at this time because of its value in the treatment of war gas poisoning, severe hemorrhage, acute altitude sickness, and shock.

The therapeutic use of oxygen is based on the existence of a state of anoxia or of tissue oxygen want. This may be produced by failure of an adequate pressure of oxygen to reach the pulmonary capillaries or by a lowered blood flow which is responsible for a disproportionately large amount of oxygen being taken out of the capillaries, resulting in a diminished oxygen pressure insufficient for normal function of the tissues. Oxygen want may, however, take place with a normal arterial saturation, as in a thrombosis of the coronary, popliteal or cerebral artery. Treatment under these circumstances makes use of the increased pressure of oxygen physically dissolved in the blood which is of special value not only in increasing the tension of oxygen through an artery that still may be partly patent but, more significantly, by increasing the tension in the collateral circulation which feeds the area of the obstructed artery. The most manifest signs of the physiologic advantages of inhalation of oxygen are diminution in pulse rate, cyanosis, dyspnea, restlessness and delirium, and the decrease in the volume of pulmonary ventilation.

Although administration of oxygen is the mainstay of this therapy, new procedures have been developed to maintain respiratory function. These include the administration of helium and of oxygen or helium-oxygen mixtures under positive pressure. The usefulness of substituting helium for nitrogen in a respirable gas mixture is due to the lower specific gravity of helium which makes it possible to breathe through constricted pulmonary passageways at almost one half the effort required for respiration of air or of pure oxygen. The decreased physical pressure necessary for the inhalation of a helium-oxygen mixture results in a lowering of the elevated negative pressure within the chest that occurs in obstructive dyspnea. Positive pressure provided in inspiration tends to prevent the excessive negative intrapulmonary pressure from exerting a suction action on the intrathoracic bronchi and pulmonary epithelium and thus is apt to inhibit the formation of mucus from the bronchi and edema from the pulmonary capillaries. Positive pressure in expiration serves the function of keeping the bronchi from advanced constriction during expiration and also of applying a direct opposing pressure on the external capillary wall, thereby retarding the tendency toward edema production and directly counteracting the internal hydrostatic pressure within the capillary.

The local application of epinephrine and neosynephrin by inhalation of the nebulized spray allows contact of these substances with the smaller bronchi locally and is frequently effective in causing cessation of bronchial spasm and a decreased swelling of the mucous membrane at a relatively low concentration of the drug in the body.

In order that the patient may benefit from inhalational therapy, the physician should be able to prescribe the concentration of oxygen to be breathed by the patient and, in the newer procedures employed, the amount of positive pressure desired or the proportion of helium in a helium-oxygen mixture.

OXYGEN REGULATION AND GAGES

Oxygen should be employed in high pressure tanks of 244 cubic feet or 6,905 liters capacity. There is no justification for the use of low pressure tanks, since there is no special "medical" oxygen and since only small quantities of oxygen can be furnished in this expensive manner. Oxygen used in medical practice is the same as industrial oxygen.

The regulator attached to an oxygen cylinder contains two gages, one which indicates the rate of flow in liters per minute and another which reveals the amount of oxygen in the cylinder. Either a variable orifice float gage or a Bourdon tube spring type regulator gage may be employed, provided the gage chosen is made by one of the reliable standard manufacturers of the equipment. The gage should be tested from time to time by measuring the rate at which the spirometer bell of a metabolism apparatus is filled at standard pressure and temperature. In attaching the regulator to an oxygen tank, the oxygen tank should first be "cracked," that is, it should be opened slightly

Prepared by a subcommittee consisting of Russell L. Cecil, M.D., chairman, Alvan L. Barach, M.D., Oswald R. Jones, M.D., and E. H. L. Corwin, Ph.D., secretary.

until the hiss of escaping gas is heard and then quickly closed. This is done to prevent the initial oxygen stream from blowing dust into the regulator.

OXYGEN TENT THERAPY FOR ADULTS

The most comfortable method of providing oxygen therapy, next to the use of the oxygen room, is in a tent with a pliofilm or other transparent canopy. However, if the tent is to fulfil its purpose, it must be able to maintain continuously the desired oxygen concentration, generally 50 per cent. The possibility of leaks developing in a unit is such that no tent should ever be used unless the oxygen concentration of the atmosphere is tested at least two or three times a day. The test is so simple and yet so essential that no physician should consent to the employment of a tent either in private practice or in the hospital unless provision is made for periodic testing and recording of the oxygen percentage of the contained atmosphere. Although a concentration of oxygen as low as 35 per cent at times will be adequate to correct anoxia, in other instances concentrations as high as 70 per cent may be desirable. It should be possible to fulfil the recommendation of the physician in respect to these oxygen concentrations in any air-tight tent. In a large oxygen tent the administration of a high flow of oxygen, for example 15 liters a minute, will result in a concentration above 50 per cent oxygen in thirty minutes. If two tanks are employed with a total inlet of 30 liters a minute, concentrations in excess of 50 per cent are obtained in fifteen minutes. When the patient is removed for examination or when for other reasons the tent canopy is opened, an increase in the flow of oxygen is indicated. There will be a saving in oxygen if the blower is stopped when ice is added to the unit.

In order to provide maximal comfort the tent should generally have a capacity of more than 8 cubic feet. The temperature inside the tent should be maintainable at the desired level by means of a cooling device. For most patients with fever a temperature between 58 and 68 F. is preferred in winter and slightly higher temperatures in summer. For older patients and infants higher temperatures are often desirable. The relative humidity should generally be maintained at between 40 and 60 per cent. When tents are ventilated by motor blown circulation which forces the air over ice, the humidity will usually be within this range. In certain conditions, such as tracheobronchitis, higher humidities and temperatures than are normally employed may be desirable. If this is the case, the circulation of the atmosphere should be lowered and the quantity of ice decreased. A spark-proof vaporizer is being developed at this time in conjunction with tent therapy. The technician should be instructed to observe and record the temperature in the tent. If the temperature goes above 70 F., the indication is that there is inadequate cooling and consequently inadequate removal of moisture also. This may be due to slow circulation of the motor blower, too little ice or ice in such small pieces as to retard circulation. Ice should be inserted in chunks the size of a grapefruit.

Within the last decade it has become apparent that the maintenance of an oxygen flow necessary to keep the oxygen concentration in a general range of 50 per cent requires a minimum flow of 9, and preferably 10, liters of oxygen a minute. This is sufficient to wash out most of the carbon dioxide produced by the patient, so that the carbon dioxide concentration is rarely above 1.5 per cent. The absence of soda lime constitutes a saving both in cost of the chemical and in the expense of supervision sufficient to compensate for the increased flow of oxygen. As a matter of fact, if lesser rates of oxygen flow are maintained and soda lime is used, there is considerable difficulty in keeping the oxygen concentration at an effectively high level, especially for patients who are seriously ill and require treatment within the tent. Because there is no valid indication for continuous stimulation of the respiratory centers, addition of carbon dioxide to oxygen is not required for most illnesses.

The oxygen concentration of the atmosphere should be tested at frequent intervals and the carbon dioxide percentage in the tent should be tested in each unit under the conditions in which the tent is ordinarily operated. Provision should also be made to test the relative humidity in the tent, although when the functional capacity of a motor blower tent has once been appraised this need not be performed daily.

In thermal circulation tents a concentration of 50 per cent may frequently be obtained by an oxygen flow below 9 liters a minute but with the inevitable accumulation of increasing concentrations of carbon dioxide as the flow is lowered below 8 liters a minute. Since a soda lime absorber would have to be added if low oxygen flows (under 8 liters) are employed, it is preferable to administer from 9 to 10 liters of oxygen a minute and give the patient the benefit of the higher oxygen concentration without the physiologic disadvantage of excess carbon dioxide in the inspired air and also without the added need for frequent carbon dioxide testing.

A closed canopy should not be put over a patient's head unless it is equipped with an adequate cooling and dehumidifying apparatus.

Although rubber or canvas canopies are still employed, the psychologic advantages of completely transparent canopies are such as to make the indication for the latter type of tent covering a strong one. Pliofilm or a suitable substitute should be used if obtainable. The modern tent is and should be noiseless, and a red light or other mechanism may be provided which remains on as an indication that the motor blower is in action.

OXYGEN TENT THERAPY FOR INFANTS

The same general principles apply to tents for infants, except that higher temperatures and higher humidities should be prescribed for very young infants. Furthermore, smaller tents may well be used. It should be recognized that infants deprived of heat by rapid circulation of cold atmosphere over them may have an abrupt fall in body temperature. A tent with an aperture at the top and with provision to admit oxygen may be used provided it is not placed near an open window or door where air currents may blow out the accumulated oxygen. It is desirable in these tents to test the oxygen concentration at a point at the level of the infant's nose. Because of the fact that infants produce so little heat, water and carbon dioxide, open top tents without an air conditioner may be employed. When closed canopies and motor driven air conditioned tents are used, the motor should be run at low speed and either no ice should be placed in the unit or only the small amount desired for the prescribed conditions of temperature and humidity.

STERILIZATION OF THE OXYGEN TENT

After the termination of each case the tent used should be washed with soap and water both inside and outside. It should then either be dipped in a solution of 1:10,000 mercury bichloride or any other efficient sterilizing solution for five minutes and washed with water or, preferably, rubbed down with 70 per cent alcohol, which is the more common practice. The use of the pliofilm canopy permits frequent replacement of it in private practice.

FIRE HAZARDS

All tents should be conspicuously labeled "Danger. No flames. No sparks." When a tent is used within a private room, it is desirable to place on the door a sign with a similar label. Oxygen regulators should also be conspicuously stamped "Do not oil." It is suggested that noninflammable pliofilm material be used in the construction of tent canopies.

Smoking should not be permitted in the room in which oxygen therapy is being conducted. No electric heating pads or electric call bells should be permitted in oxygen tents. Visitors should be warned by word of mouth not to light matches and to observe the regulations, since some do not speak English or do not read the instructions.

NASAL CATHETERS

There are several effective methods of administering oxygen through the nose by employing a nasal catheter either in the nasopharynx or in the oral pharynx or, in some instances, by the use of a nasal metal tube which just enters each nostril. A soft rubber nasal catheter is generally preferred to the metal nasal tube. The oxygen is first passed through approximately 3 inches of water to prevent drying of the mucous membranes. A lubricated nasal catheter number 10 or 12 French is inserted into the nostril for a distance of approximately 3 inches, that is, up to but not touching the posterior wall of the nasopharynx. Five liters of oxygen a minute generally provides 37 per cent oxygen in the inspired air. A single catheter may be changed from one nostril to the other if irritation should occur. The terminal inch of the catheter should be perforated with four small holes in order to prevent a single stream of oxygen impinging on one localized area of the mucous membrane.

If the catheter is passed down into the oral pharynx opposite the glottis, a concentration of 42 per cent oxygen may be obtained in the inspired air at a flow of 5 liters a minute. When the catheter is used in the oral pharynx, it is important to remember that oxygen may pass into the stomach and distend the abdomen if the catheter is placed lower than the uvula. If the pharyngeal position of the catheter is adopted, 7 liters of oxygen a minute to supply concentrations of oxygen in excess of 50 per cent may be used if no sensation of discomfort is produced. The nasal catheter should be lubricated with KY jelly or petrolatum each time it is inserted. The catheter should be removed at least twice in twenty-four hours for cleaning and, at the termination of the case, should be cleansed and sterilized. This is important, as otherwise the small holes in the terminal inch of the catheter may be plugged and oxygen may escape through one single orifice, thus producing irritation of the nasal mucous membrane. When a patient, after insertion of the catheter in the oral pharynx, swallows a bolus of air, the inference is that the catheter has been inserted too far; it is then withdrawn until no gas is taken into the stomach during deglutition.

OXYGEN MASKS

Oxygen masks are especially suitable for administration of high concentrations of oxygen from 50 to 100 per cent. For application in either the nasal or the oral pharynx, the nasal catheter is generally more comfortable for long continued use and just as effective as the oxygen mask if concentrations below 50 per cent are prescribed. The oxygen tents with transparent canopies and air conditioning cabinets are generally more comfortable for the administration of moderate oxygen concentrations, such as between 40 and 60 per cent. Within recent years it has become apparent that pure oxygen is not irritating to human pulmonary epithelium when administered by a mask for two days, and in all probability for four days. The fact that the mask is removed from time to time in order to provide food or that the face may be washed or for other reasons may be responsible for this exceptional tolerance of 100 per cent oxygen. At any rate, the previous warnings regarding the danger of pulmonary edema from inhalation of these very high oxygen atmospheres were based on experiments on animals which were kept in air-tight chambers continuously for three or four days. Since clinical evidence has been forthcoming from a number of hospitals indicating that concentrations of oxygen between 70 and 100 per cent have been used without damage to the lung for periods of from two to five days, there has been opened a new field for the mask in which a large increase in physically dissolved oxygen may be of crucial value in such conditions as shock, severe hemorrhage and imminent cardiac failure.

There are two masks available, the B. L. B. (Boothby-Lovelace-Bulbulian) and the Barach-Eckmann injector meter mask. In the B. L. B. mask a well fitting rubber nasal or oral-nasal mask is attached to the face and from it is suspended a small bag in which a moderate amount of rebreathing takes place. Two sponge rubber disks placed in the center of the mask serve as a combination inspiratory and expiratory valve. During inspiration there is sufficient resistance in the sponge rubber to prevent a free flow of air into the mask. When the rebreathing bag is emptied, air is drawn through the sponge disk. During expiration, first the rebreathing bag is filled with the exhaled air and the remainder of expired air then passes through the sponge rubber disk into the outer atmosphere.

During increased ventilation, as in severe dyspnea, the resistance imposed by breathing through the sponge rubber is naturally increased. This is especially significant during the inspiratory cycle if flows of oxygen under 6 liters a minute are used. It must also be pointed out that a flow of oxygen at a rate as low as 2 to 4 liters a minute will be accompanied by sufficient rebreathing to produce a carbon dioxide percentage in the inspired air of approximately 2 per cent. With this mask it is generally desirable to use a high flow of oxygen, as at the rate of from 7 to 10 liters a minute, in order to eliminate the inspiratory resistance and the increased carbon dioxide in the inspired air.

In the injector mask a delicate inspiratory valve is placed between the mask and a large, light latex bag

which prevents any rebreathing and simply serves as a collecting bag for oxygen. A light rubber flutter expiratory valve is placed in front of the mask for exit of the exhaled atmosphere. This mask operates at minimal resistance during both high and low oxygen flows. An injector is attached to the regulator, which makes possible the administration of any oxygen concentration desired from 40 to 100 per cent. By use of different sized apertures in the injector, a variable amount of atmospheric air is pulled into it because of the negative pressure created by the stream of oxygen passing through it into the rubber tubing. Calibration of these orifices makes possible the instantaneous provision of the desired oxygen concentration with an error of not more than ± 3 per cent. If the administration of low flows of oxygen and the exclusion of carbon dioxide in the inspired air are called for, the injector mask is most suitable for this purpose. If carbon dioxide of varying percentages is prescribed, the inspiratory valve in this mask may be removed to allow rebreathing, or the B. L. B. mask may be employed. The latter mask may be obtained in two sizes. It is essential that in cases presenting obstructive dyspnea a minimal inspiratory resistance is present. The rate of flow of oxygen from the regulator may be varied from 4 to 15 liters a minute, depending on the concentration of oxygen desired and the desirability of avoiding resistance from the apparatus itself. The employment of less than 4 liters a minute is rarely indicated except for young children, for whom lower flows may be adequate.

Although these newer types of masks are comfortable for a large number of patients, it must be recognized that their continuous use becomes objectionable to a good many others. When discomfort prevents the continuous administration of oxygen by mask, a shift should be made to the oxygen tent, if it is feasible, or, if not, to the nasal catheter.

After use, the mask should be scrubbed thoroughly with soap and water and boiled, or immersed or washed in a 70 per cent alcohol solution.

THE OXYGEN MASK METERED FOR POSITIVE PRESSURE

The injector mask may be obtained equipped with a metal disk which surrounds the expiratory flutter valve and contains on its external surface five orifices of different diameters. When the largest sized orifice is employed, expiration proceeds naturally without pressure. When the disk is turned to the orifices of smaller size, the patient exhales under a positive pressure of 1, 2, 3 or 4 cm. of water, depending on the size of the orifice.

Provision of positive pressure during expiration is specifically indicated for the treatment of pulmonary edema, either during the course of cardiorespiratory illness or as a specific remedy for pulmonary irritants, such as chlorine gas or the fumes of nitric acid. In treating pulmonary edema it is customary to begin with high pressures, such as 4 cm., and gradually lower the pressure to 2 and 1 cm. of water. From 40 to 100 per cent oxygen is employed. The injector attached to the regulator is turned to the oxygen percentage desired, and the flow from the regulator is adjusted at that rate which prevents the collecting bag from collapsing at the end of inspiration. It is desirable to have the injector one third full of water so that the stream of oxygen may pick up some moisture as it passes into the mask.

The relative humidity of pure oxygen passing at a flow of from 8 to 10 liters a minute through the injector partially filled with water is approximately 20 per cent at 70 F. The inspired oxygen is additionally moistened by the inner surfaces of the mask, which are wet with the saturated water vapor resulting from expiration, so that the ultimate relative humidity of the inspired oxygen is approximately 45 per cent. If a still higher relative humidity is desired during inhalation of 100 per cent oxygen, the injector is removed and a water bottle attached to the regulator, so that the stream of oxygen will pass upward through at least 3 inches of water before entering the mask.

Positive pressure is employed also to prevent or control the oozing that takes place from the tracheobronchial tree following tracheotomy in cases of previously existing laryngeal obstruction. In this instance the tracheotomy tube is prolonged so that inspiration may take place through a flutter valve and expiration proceed through an expiratory valve into a water bottle at pressures which generally begin at from 4 to 5 cm. of water and are gradually lowered during a period of twelve hours to from 1 to 2 cm. of water.

Positive pressure respiration appears to be contraindicated in shock in which the venous return to the heart is retarded. The increased intrapulmonary pressure of from 2 to 4 cm. of water may further diminish the flow of blood into the right auricle. When peripheral circulatory failure is suspected the blood pressure should be followed at fifteen minute intervals and the pressure reduced or discontinued if a fall greater than 10 mm. of mercury takes place in the systolic pressure following application of breathing under positve pressure.

THE HELIUM-OXYGEN HOOD

Although helium-oxygen therapy may be carried out by means of mask oxygen apparatus, the helium-oxygen hood is the only effective apparatus for administering from 20 to 30 per cent oxygen and from 80 to 70 per cent helium under a positive pressure during inspiration as well as expiration. The apparatus consists of a hood with a removable rubber collar, which fits around the neck, and an air conditioning cabinet. The conditioning cabinet contains two Barolyme carbon dioxide absorbers which are placed in ice water, a motor blower unit and a rheostat for controlling the velocity of air circulating through the hood. To the hood is attached a pressure control water valve that consists simply of a rubber tube with a glass connection leading into a water bottle. The length of the glass tube immersed in the water determines the pressure to which the head of the patient, and therefore the intrapulmonary respiratory passageway, is exposed. This apparatus is employed for the treatment of severe bronchial asthma and for obstructive dyspnea produced by lesions in the tracheobronchial passageway.

Since this is a closed circuit apparatus in which special precautions are taken to avoid all leaks, in order that no nitrogen may be admitted into the helium-oxygen atmosphere, it is especially important to provide efficient cooling and dehumidification and to use a soda lime absorbent to prevent the accumulation of carbon dioxide.

If helium is not available, the helmet may be employed with the administration of 100 per cent

oxygen for the treatment of both asthma and obstructive dyspnea generally. Inhalation of oxygen under pressure during the inspiratory cycle is especially apt to relieve severe dyspnea due to laryngeal or tracheal constriction. The helium-oxygen hood is used also for the treatment of pulmonary edema, at first with a relatively high pressure of from 5 to 6 cm. of water, then with pressures gradually reduced to 2 and 1 cm., and finally to atmospheric pressure.

Since helium is an inert gas it should not be employed without previous admixture with oxygen in tanks containing 20 to 25 per cent oxygen and 80 to 75 per cent helium respectively. If separate tanks of oxygen and helium were employed to supply a hood or mask apparatus, inadvertent stoppage of the oxygen supply would result in progressive elevation of the helium concentration of the contained atmosphere, with danger of asphyxia to the patient.

THE ADMINISTRATION OF 5 TO 10 PER CENT CARBON DIOXIDE IN OXYGEN

The administration of 5 to 10 per cent carbon dioxide in oxygen is useful in carbon monoxide poisoning and other clinical conditions such as electric shock, morphine poisoning and drowning in which the respiratory center may be depressed. Carbon dioxide-oxygen inhalation has also been employed in massive collapse of the lungs, in order to stretch the bronchi and perhaps loosen a tenacious plug of mucus, and for short periods after operations to expand the lungs and bronchi in the belief that atelectasis may be less likely to take place. It is particularly useful in intractable hiccup. For this purpose a tank of either 90 per cent oxygen and 10 per cent carbon dioxide or 93 per cent oxygen and 7 per cent carbon dioxide may be employed either with a B. L. B. or an injector mask for short periods of two or three minutes or until an increase in pulmonary ventilation has taken place sufficient to relieve the condition for which it was intended. It must be borne in mind that prolonged administration of carbon dioxide will bring about toxic symptoms, such as headache, nausea and, if concentrations above 10 per cent are employed too long, convulsions.

ADMINISTRATION OF VAPORIZED SOLUTIONS OF EPINEPHRINE AND NEOSYNEPHRIN HYDROCHLORIDE

It has been found convenient to use a nebulizer with a hand bulb to vaporize 1:100 epinephrine and 1 per cent neosynephrin hydrochloride. Since the vaporization of relatively large amounts of these drugs has been shown to be valuable in the treatment of severe bronchial asthma, the high pressure tank rather than the hand bulb should be used. One cc. of 1:100 epinephrine or 1 cc. of 1 per cent neosynephrin hydrochloride may be inserted into one of the openings in a glass nebulizer and a tube from an oxygen tank connected to the glass outlet. The oxygen from the tank is then turned to 5 liters a minute and the wide end of the nebulizer held between the teeth with the mouth wide open. The nebulizer is rinsed with warm water after use to prevent clogging. It is generally desirable to use a warm mouth wash and gargle after spraying with epinephrine solutions to prevent drying of the throat. This method of supplying the bronchi and alveoli with nebulized solutions may be used for the administration of other drugs, such as diaminosulfone glucoside.

TECHNICIANS

The technics of inhalational therapy must be skilfully administered if use of the therapy is to be of benefit to the patient. Because of the complexity and diversity of the more modern apparatus, many physicians prefer to have technicians attend to the mechanical details involved. Such technicians should be properly trained and supervised. It is therefore suggested that appropriate courses be given for the training of inhalational therapy technicians and nurses who assist in these procedures.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS PREVIOUSLY PUBLISHED ITS CONSIDERATION OF A COD LIVER OIL PREPARATION (THE JOURNAL, OCT. 24, 1936, P. 1384), BUT BECAUSE OF RENEWED INTEREST IN THIS CLASS OF AGENTS FOR THE TREATMENT OF BURNS AND THE ACCELERATION OF WOUND HEALING AND IN THE VALIDITY OF CERTAIN ADVERTISING CLAIMS, PUBLICATION OF THE FOLLOWING STATUS REPORT WAS DEEMED ADVISABLE. THIS REPORT REVEALS THAT MUCH WORK HAS BEEN PUBLISHED ON THE SUBJECT BUT, UNFORTUNATELY, THE LACK OF ADEQUATE CONTROLS, OR REPORTS ON SUCH CONTROLS, HAS HINDERED GREATLY A TRUE EVALUATION OF THE STATUS OF COD LIVER OIL IN THE MEDICAL ARMAMENTARIUM AS FAR AS TOPICAL APPLICATION IS CONCERNED. WHILE SOME INTERESTING OBSERVATIONS HAVE BEEN RECORDED, CONSIDERABLE EXPERIMENTATION REMAINS TO BE DONE. IN VIEW OF THE CURRENT CONFLICTING OPINIONS AND LACK OF SUBSTANTIATING EVIDENCE THE COUNCIL IS OF THE OPINION THAT THERE REMAIN TOO MANY UNANSWERED QUESTIONS TO WARRANT ACCEPTANCE OF COD LIVER OIL PREPARATIONS FOR EXTERNAL USE AT THIS TIME, BUT IT PRESENTS THE FOLLOWING STATEMENT TO OFFER TO THE MEDICAL PROFESSION A CONCISE REVIEW OF THE PRESENT STATUS OF SUCH MEDICAMENTS AND TO SUGGEST THE NEED FOR FURTHER CAREFULLY CONTROLLED OBSERVATIONS. AUSTIN E. SMITH, M.D., Secretary.

A STATUS REPORT ON THE EXTERNAL USE OF COD LIVER OIL

Löhr [1] was the first to publicize widely the use of cod liver oil externally. He employed an ointment containing one part of cod liver oil mixed with two parts of petrolatum in treating burns, abscesses, wounds, ulcers and osteomyelitis. He reported unusual success, especially in the rapid epithelization of large areas and the conversion of unhealthy necrotic areas to clean, bacteria free wounds. Löhr stated that he found skin grafting unnecessary even when large areas were denuded. Since the publication of Löhr's original articles, many reports have appeared in the literature. Thus, Lücke [2] used Löhr's treatment successfully in furunculosis, abscesses, infected wounds and ulcers. Later he added bee honey to the ointment and felt that the results were even better. Buchheister [3] also had good results from the latter unguent in infected surgical wounds, furunculosis, carbunculosis, osteomyelitis and mastoiditis. Kirschner [4] disagreed with Löhr's claims. He found zinc ointment to be more effective than cod liver oil, which he reported as actually harmful in some instances. He marked as false the conclusion that under local cod liver oil treatment all wounds epithelize and no skin grafting is necessary. Steel [5] employed

1. Löhr, W.: Zentralbl. f. Chir. **60:** 1611 (July 8) 1933; Ueber die Lebertransalbenbehandlung (mit und ohne Gipsverband) bei frischen Verletzungen, Verbrennungen und phlegmonosen Entzündungen, ibid. **61:** 1686 (July 21) 1934; Die Behandlung von schlecht heilenden, ulzerosen Gliedmasstumpfen mit grossen Gewebsdefekten (nach Verkohlung, Erfrierung und Amputation) mit dem Lebertran-Gipsverband, ibid. **61:** 1815 (Aug. 4) 1934; Die Wundbehandlung schwer heilbarer Wunden unter Benutzung von Lebertran, Therap. d. Gegenw. **75:** 444 (Oct.) 1934; Die Behandlung grosser, flachenhafter Verbrennungen 1, 2 und 3 Grades mit Lebertran, Chirurg. **6:** 263 (April 1) 1934; Der Lebertran bei der ausseren Behandlung von Wunden, Deutsche med. Wchnschr. **60:** 561 (April 13) 1934; Die Behandlung der akuten und chronischen Osteomyelitischer Rohrenknocken mit Lebertrangips, Arch. f. klin. Chir. **180:** 206, 1934; Treatment of Acute and Chronic Osteomyelitis of Tubular Bones by Means of Cod Liver Oil and Plaster Casts, Deutsche med. Wchnschr. **62:** 997 (June 19) 1936. Löhr and Treusch.[20]

2. Lücke, H.: Deutsche med. Wchnschr. **61:** 967 (June 14) 1935.

3. Buchheister, H.: Erfahrungen mit Honig und Lebertran in der Wundbehandlung, München. med. Wchnschr. **82:** 1612 (Oct. 4) 1935.

4. Kirschner, M.: Bedeutung der Vitamine fur die Chirurgie, Arch. f. klin. Chir. **189:** 63 (Aug. 30) 1937.

5. Steel, J. P.: Cod Liver Oil Treatment of Wounds, Lancet **2:** 290 (Aug. 10) 1935.

gauze saturated with crude cod liver oil in the treatment of minor and severe burns and found it suitable for indolent ulcers, deep abrasions and infection. He believed the higher the vitamin content the better the results and used his crude cod liver oil treatment routinely for burns. Schaer [6] found cod liver oil satisfactory in the secondary healing of wounds but felt that its use in osteomyelitis required further investigation. Balachovski and Ratcheviski [7] and Balachovski [8] used carotene in a paraffin base for burns. Iost and Kochergin [9] employed a cod liver oil ointment in 263 cases of superficial and suppurating wounds, open amputation stumps, ulcers, frost bites and traumas. Mason [10] advocated cod liver oil to stimulate indolent burns. On the other hand, MacCollum [11] used cod liver oil and other unguents in unhealed burns and found that all had about the same effect. Wakeley,[12] in discussing war burns, spoke among other forms of treatment of cod liver oil for burns of the face. Meherin and Schoemaker,[13] reporting on the treatment of cement burns, stated that, once clean granulations have started, cod liver oil ointment should be used. Driver, Binkley and Sullivan [14] used an ointment containing cod liver oil 88 per cent and white wax 12 per cent and an ointment of white petrolatum to which was added 2,000 U. S. P. units of oil soluble carotene per gram. They treated 25 cases of varicose ulcers, 4 of erythema induratum and 3 indolent ulcers. The results were generally more satisfactory than those obtained by other methods. Stevenson [15] has reported good results with cod liver oil ointment in the treatment of burns of the cornea, eyes and lids. Hardin,[16] after reviewing the entire subject and reporting his own experience in 396 cases of various types of wounds, felt that cod liver oil ointment was an effective method of local wound therapy. Such treatment, according to this author, is applicable to both clean and infected wounds and to new and old burns of major severity. Aldrich [17] found cod liver oil ointment to give excellent results in the treatment of burns, wounds, indolent ulcers and pruritus ani and vulvae, while Brandaleone [18] reported that such ointments promote the healing of ulcers of the feet in patients with diabetes.

Many similar clinical reports could be cited. In general, such reports stress the impression that cod liver oil applied locally produces a definite leukocytic response with rapid liquefaction of necrotic material, suppression of local infection and stimulation of granulation tissue and of epithelization, with rapid healing and minimal scarring. Unfortunately well controlled clinical investigations are remarkable by their scarcity, while only a few studies of the comparative effect of cod liver oil in promoting the healing of experimental wounds in animals have appeared. Puestow, Poncher and Hammatt [19] showed that burns in guinea pigs and rabbits healed 25 per cent faster under cod liver oil therapy than with tannic acid. There was no indication in this report that the results obtained were statistically significant. Getz [20] found that experimentally produced tuberculous skin lesions in guinea pigs healed more rapidly when treated with cod liver oil than when treated with paraffin, lanum or cottonseed oil. Brandaleone and Popper [21] found the rate of healing of elliptic wounds in vitamin A deficient rats (produced by clipping away a portion of the skin with scissors) significantly higher if cod liver oil was locally applied or given orally than if the wounds were untreated or treated with linseed oil. No significant differences in the rate of healing of such treated and untreated wounds in normal rats was found. Puestow and his collaborators [19] could find no histologic evidence that the scars of healed burns following treatment with cod liver oil were different from those following other treatment. Brandaleone and Popper [21] studied microscopically the scars occurring in their animals but report no differences which may have occurred as a result of varying treatments.

The mechanism of any local action which cod liver oil may produce remains unknown. Most clinical reports, beginning with those of Löhr, have assumed on an empiric basis that the activity noted was due to the vitamin content of the oil. Löhr and Unger [22] tested the efficacy of various cod liver oil fractions in promoting the healing of experimental wounds in guinea pigs. No data were given, but they concluded that cholesterol, squalene and saturated fatty acids were ineffective, while vitamins A and D and the unsaturated fatty acids promoted healing. Concentrations of the vitamins higher than those found in cod liver oil were said to be detrimental. Lauber [23] found that vitamin A applied locally produced no acceleration of wound healing and in concentrated amounts retarded it. He also reported that, while small quantities of vitamin D produced a slight acceleration, large doses inhibited it. Rötth [24] found that the local application of oils containing vitamin A prevented or cured the keratomalacia of vitamin A deficient rats. However, cod liver oil treatment caused no more rapid healing of artificially produced abrasions of rabbits' corneas than did liquid petrolatum. Getz [20] fractionated cod liver oil in an effort to determine the principle responsible for the more rapid healing of tuberculous ulcers in guinea pigs. The fatty acid fraction of the cod liver oil was found to be nonhealing. The active agent was concentrated in the "nonsaponifiable residue," since experimentally it caused faster healing than the whole oil. This nonsaponifiable residue was further fractionated. The precipitate of heavy sterol was found to be inert, and the filtrate designated the "vitamin fraction" proved to be active. This so-called "vitamin fraction" had two known constituents—vitamins A and D—and numerous unknown substances. The author compared as to healing properties three different oils, varying greatly in their content of vitamins A and D: halibut liver oil with 50,000 A and 200 D units, tuna liver oil with 70,000 A and 88,000 D units and cod liver oil with 1,800 A and 175 D units per gram. Assuming the oils to be comparable in other respects, if vitamin A was the factor, halibut and tuna liver oils should have been more effective; while, if vitamin D was the desired agent, tuna liver oil should have been best. Cod liver oil proved to be superior to either of the other agents. In the report of Puestow and his collaborators [19] the healing of electrocautery burns (in pigs and rabbits) was studied following treatment with various vitamin containing oils. While the cod liver oil treated lesions healed 25 per cent faster than those untreated or treated with 5 per cent tannic acid or olive oil, those treated with ointments of varying vitamin content showed approximately the same healing as with cod liver oil. These high vitamin ointments were one containing no vitamin A but containing irradiated ergosterol in oil to give 625,000 units of vitamin D per gram of ointment, one containing fish liver oil to give 28,125 units of vita-

6. Schaer, H.: Erfahrungen mit Unguentolan, Schweiz. med. Wchnschr. **65:** 724 (Aug. 10) 1935.
7. Balachovski, S., and Ratchevski, F.: Recherches sur quelques propriétés nouvelles du carotene. Existe-t-il une insuffisance locale en vitamines? Bull. Soc. chim. biol. **16:** 220 (Feb.) 1934.
8. Balachovski, S.: Sur la possibilité d'insuffisances locales en vitamines; considérations théoriques et application thérapeutique, Presse méd. **42:** 1404 (Sept. 8) 1934.
9. Iost, V. I., and Kochergin, I. G.: Clinical and Laboratory Evaluation of Cod Liver Oil in Therapy of Wounds, Nov. Khir. Ark. **34:** 476 (No. 136) 1935; abstr. J. A. M. A. **106:** 586 (Feb. 15) 1936.
10. Mason, R. L.: Preoperative and Postoperative Treatment, Philadelphia, W. B. Saunders Company, 1937.
11. MacCollum, D. W.: Early and Late Treatment of Burns in Children, Am. J. Surg. **39:** 275 (Feb.) 1938.
12. Wakeley, C. P. G.: War Burns and Their Treatment, Practitioner **146:** 27 (Jan.) 1941.
13. Meherin, J. M., and Schoemaker, T. P.: Cement Burn: Its Etiology, Pathology and Treatment, J. A. M. A. **112:** 1322 (April 8) 1939.
14. Driver, J. R.; Binkley, G. W., and Sullivan, Maurice: Cod Liver Oil and Carotene Ointments in the Treatment of Indolent Ulcers: Preliminary Report, Urol. & Cutan. Rev. **42:** 587 (Aug.) 1938.
15. Stevenson, Edgar: Cod Liver Oil as Local Treatment for External Affections of Eyes, Brit. J. Ophth. **20:** 416 (July) 1936.
16. Hardin, P. C.: Cod Liver Oil Therapy of Wounds and Burns, South. Surgeon **10:** 301 (May) 1941.
17. Aldrich, R. H.: Cod Liver Oil Ointment in Surgery, Indust. Med. **11:** 153 (April) 1942.
18. Brandaleone, Harold: The Effect of the Direct Application of Cod Liver Oil on the Healing of Ulcers of the Feet in Patients with Diabetes Mellitus, Ann. Surg. **108:** 141 (July) 1938.
19. Puestow, C. B.; Poncher, H. G., and Hammatt, Harold: Vitamin Oils in the Treatment of Burns: An Experimental Study, Surg., Gynec. & Obst. **66:** 622 (March) 1938.
20. Getz, H. R.: Cod Liver Oil Therapy in Experimental Tuberculosis, Proc. Soc. Exper. Biol. & Med. **38:** 543 (May) 1938.
21. Brandaleone, Harold, and Popper, Edith: The Effect of Local and Oral Administration of Cod Liver Oil on the Rate of Wound Healing in Vitamin A-Deficient and Normal Rats, Ann. Surg. **114:** 791 (Oct.) 1941.
22. Löhr, W., and Unger, F.: Tierexperimentelle Untersuchungen über die Wundheilung mit Lebertran und die Wirkung seiner Bestandteile, Arch. f. klin. Chir. **189:** 405 (Aug.) 1937.
23. Lauber, H. J.: Weitere experimentelle Untersuchungen über die Beziehungen der Vitamine zur Wundheilung, Beitr. z. klin. Chir. **161:** 565, 1935.
24. de Rötth, A. F. M.: Local Action of Oils Containing Vitamin A, Arch. Ophth. **24:** 281 (Aug.) 1940.

min A and 46,875 units of vitamin D per gram of ointment, and one containing fish liver oil to give 237,500 units of vitamin A and 1,250 units of vitamin D per gram of ointment. The ointment containing irradiated ergosterol gave startling evidence of toxicity when used on rabbits: 13 of 15 such animals died in less than a week. Dann, Glücksmann and Tansley,[25] using technics and standards considerably more rigid than in most such reports, studied the rate of collagen and epithelial regeneration of "standard" wounds in rats when treated with various agents. The rapidity of healing of such wounds when untreated was compared with that seen when the following oils were used as a local treatment: cod liver oil (two samples); the distillate and the residue of a molecular distillation of cod liver oil; vitamin A naphthoate; vitamin A in coconut oil; coconut oil; peroxidized Arachis oil; Arachis oil; linoleic acid; methyl linoleate, and liquid paraffin. In most cases 12 or more animals were used in each group. It was found that collagen regeneration was stimulated to a varying degree by all the substances. Hypertrophic collagen regeneration after Arachis oil interfered with epithelial regeneration. Epithelial regeneration was promoted by linoleic acid only; it was delayed by all other substances except liquid paraffin and one sample of cod liver oil. Such results cast grave doubts as to whether the local application of vitamins A and D has any effect at all on wound healing, provided always that no general avitaminosis A or D exists. The experiments of Brandaleone and Popper[21] do not answer this question, as local cod liver oil treatment produced no increase in the rate of healing of the normal rats of their series.

Löhr and Treusch[26] believed cod liver oil to possess bacteriostatic and bactericidal qualities. They found oil inoculated with staphylococci, streptococci and colon bacilli to be sterile after twenty-four hours. Löhr stated that cod liver oil is always sterile. Tumanskiy and Yatsevich[27] found that growth of streptococci and staphylococci in sterilized and nonsterilized cod liver oil ceased after one hour and six hours respectively. If sterile petrolatum was added to cod liver oil, bacteria grew for seventy-two hours. In sterile petrolatum alone, growth was prolonged for fifteen days. Kummell and Jensen[28] examined different specimens of Löhr's preparation (one part of cod liver oil to two parts of petrolatum) and gypsum dressings after their removal, took cultures of them and found no interference with cultural growth. Regularly, cultures from the bottom of the oil deposits were sterile. Fresh superficial wounds treated with cod liver oil showed a bacterial growth. The paper of Driver, Binkley and Sullivan,[14] which showed that cod liver oil required the addition of phenylmercuric benzoate 1:1,000 or phenylmercuric borate 1:2,500 before inhibition of bacteria was produced, suggests that its disinfectant properties are definitely limited. Yet von Drigalski[29] claimed that cod liver oil interferes with the growth of organisms cultivated from the ground and from the feces and sputum. Lichtenstein[30] found that in a nutrient medium staphylococci succumbed under cod liver oil in two weeks, Escherichia coli was resistant to cod liver oil, the addition of vitamins A and D to cod liver oil did not influence its action, and both staphylococci and Escherichia coli survived indefinitely under liquid paraffin. In the absence of a nutrient medium, liquid paraffin had no influence on the vitality of the organisms for the time observed (thirty-five days), olive oil killed bacteria suspended in it in seven to ten days, while cod liver oil had the same effect in seventeen to twenty-two hours and boiled linseed oil in one to one and one-fourth hours. Irradiated cod liver oil had a greater bactericidal effect under such conditions than before irradiation. The author found an inverse relationship between the length of time required to kill the bacteria and the amount of peroxide present in these oily preparations. He was unable to rule out the possibility that other substances might play a part.

There are differences of opinion in the literature concerning the strength of cod liver oil which should be employed in ointments applied locally. With no conclusive evidence on which to base their opinions, most workers apparently feel that the higher the percentage of cod liver oil, up to 80 per cent, the better the ointment.

The complete immobilization of the affected part was an integral part of the treatment described by Löhr. Hardin[16] stated that his conception of the cod liver oil treatment of wounds closely resembles Orr's closed petrolatum treatment of compound fractures[31] and the closed plaster treatment of war wounds described by Trueta.[32] Many other reports indicate that the success of cod liver oil dressings is dependent in part on such immobilization and the fewer dressings required. The relative freedom from pain during the changing of dressings is thought by some to be a factor to be considered. MacCollum[11] thought the pressure dressings more important in the treatment of burns of children than the type of ointment used.

Most writers emphasize that the use of cod liver oil does not invalidate the accepted methods of routine wound care such as careful débridement, maintenance of blood volume, combating anemia and treatment of general disease. Hardin[16] warns that cod liver oil must be used with judgment in badly contaminated wounds and is not immediately applicable to acute inflammatory lesions, where the usual surgical measures are indicated. Finally, it is agreed that early skin grafting is, above all, a necessity.

In summary, it may be said that there is a significant number of clinical reports favorable to the use of cod liver oil ointments in the local treatment of burns of all types, of wounds and of ulcers. Burns in the "indolent stage" and indolent ulcers are said to be especially benefited by local cod liver oil treatment, when dressings are left in place forty-eight hours. Most workers are agreed that local infection diminishes, necrotic material is liquefied and growth of granulation tissue and epithelization are stimulated. Unfortunately there is a surprising and regrettable lack of control in such studies. The difficulty of evaluating such reports is emphasized by the Youngs and Fisher,[33] who criticized the common practice of basing claims on insignificant data without respect to the biologic variations which count so much in the healing of a wound. The few experimental studies reported are not conclusive; indeed, the more recent and better controlled work on animals has failed to show any advantage of cod liver oil ointment over other ointments. The therapeutic constituents of cod liver oil aside from vitamins are still unknown. The concept that the possible stimulating properties of cod liver oil rest in its vitamin content is purely empiric; studies predicating the bacteriostatic and bactericidal activity of cod liver oil are controversial. Few reports of toxicity from the use of cod liver oil ointments have appeared. It is apparent that such ointments can serve the function of a stimulating ointment and several reports attest their beneficial effect on indolent ulcers. However, their use should not violate recognized surgical principles; such preparations do not obviate the necessity for early and careful skin grafting or of other recognized medical agents for the treatment of burns and wounds.

At the time of considering this report the Council had before it the presentation of two commercially available cod liver oil preparations for topical application. After due consideration the Council voted that any favorable action on such agents must await further evidence. Accordingly, the firms were notified of the Council's decision.

25. Dann, Lotte; Glücksmann, Alfred, and Tansley, Katharine: Experimental Wounds Treated with Cod Liver Oil and Related Substances, Lancet **1**: 95 (Jan. 24) 1942.

26. Löhr, W., and Treusch, K.: Die Wirkung des Lebertrans und der Lebertransalbe auf Wundeitererreger, Zentralbl. f. Chir. **61**: 1807 (Aug. 4) 1934.

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30. Lichtenstein, M.: Cod Liver Oil Dressings; Their Mode of Action, Lancet **2**: 1023 (Nov. 11) 1939.

31. Orr, H. W.: Early Treatment of Gunshot Wounds and Fractures, J. Indiana M. A. **33**: 442 (Sept.) 1940.

32. Trueta, Joseph: "Closed" Treatment of War Fractures, Lancet **1**: 1452 (June 24) 1939.

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SATURDAY, MARCH 6, 1943

THE MEDICAL DEPARTMENT OF THE ARMY

When the medical history of World War II is written the year that elapsed following the treacherous attack by Japan at Pearl Harbor will be recognized as one in which the Medical Department of the United States Army was expanded tremendously in personnel, organized units, supplies and responsibilities and in which it met all these demands quietly and efficiently. Now with more than thirty-five thousand medical officers, with hundreds of thousands of medical corps men, with double the number of general and station hospitals and well-nigh triple the bed capacity, it stands ready to meet any new obligations that may be placed upon it. During the year the only serious incident from a medical point of view was the jaundice associated with inoculation against yellow fever. The first week of February 1943 found atypical pneumonia and meningitis most prominent of the infectious diseases but even these were scattering with a few cases here and there and only a score or slightly more of cases of either in the few camps most seriously affected. From July 1942 the maximum admissions for venereal disease had reached less than 1 per thousand, and admissions for both gonorrhea and syphilis had fallen in February 1943 below levels of November 1942.

The remarkable records here cited are the actual evidence of the effectiveness of the organization of the Office of the Surgeon General to meet every contingency. In January 1941 a Central Epidemic Control Board was established including such specialists from civilian life as Drs. Francis G. Blake of Yale, O. H. Perry Pepper, Pennsylvania, Alphonse R. Dochez, Columbia, E. W. Goodpasture, Vanderbilt, Kenneth F. Maxcy, Johns Hopkins, A. J. Warren and Wilbur F. Sawyer of the International Health Division of the Rockefeller Foundation, Oswald T. Avery of the Rockefeller Institute and E. S. Robinson of the Massachusetts Department of Health. A special commission on influenza is headed by Dr. Thomas Francis Jr. of Michigan, one on pneumonia by Colin M. McLeod of New York University, one on hemolytic streptococcus disease by M. H. Dawson of Columbia, one on measles by Joseph Stokes Jr., Pennsylvania, one on meningitis by Perrin Long, Johns Hopkins, and one on neurotropic virus diseases by John R. Paul, Yale. Dr. Stanhope Bayne-Jones of Yale heads the commission on epidemiologic survey.

To head services in the Office of the Surgeon General have come Brig. Gen. Hugh Morgan of Vanderbilt for medicine, Brig. Gen. Fred Rankin for surgery, Col. Esmond R. Long for tuberculosis. The manner in which these distinguished physicians from civilian life have been drawn into military service in positions of leadership, along with Brig. Gen. Elliott Cutler, now abroad, and many others who serve in organized units has been an inspiration to the many thousands of young men who know that they will find standards of medical service in our armed forces well up to those of civilian practice.

Notwithstanding the speed with which this great medical army has been assembled, the difficulties of adjustment of personnel have been slight. Col. George Lull, whose report was published in THE JOURNAL last week, has merited the friendship now held for him by many thousands of civilian physicians who would have found transition to a military status far more difficult without his unfailing tact and courtesy.

Under Brig. Gen. C. C. Hillman, professional services have been standardized utilizing the wealth of talent assembled by the Division of Medical Sciences of the National Research Council. Facilities have been organized by which every person entering the military service is given an x-ray examination of the chest and the roentgenogram is filed permanently with his record. Hundreds of thousands of young men of doubtful physical status have had their records reviewed by this division.

Under Col. James S. Simmons epidemiologic studies have been made which will lead to adequate protection of our young men regardless of the theater of war into which they may be called. Far too often the public thinks of the army doctor only as one who treats wounds on the battlefield. However, insect control, delousing, sanitary dishwashing, development of safe water supplies, selection of clothing for various climates, occupational hygiene and venereal disease control come also under the medical department. Then too the dental division, meat and dairy inspection, care of animals, nursing and physical therapy are parts of the complex organization which has functioned so efficiently under Surg. Gen. James C. Magee in the year of war that has passed.

Today wintertime ailments such as colds, influenza, pneumonia and measles are well below the five year average rate of cases in the Army, even though rates for the civil population in some parts of the country are above the five year average for the country. Venereal disease is substantially less than during World

War I, and the syphilis rate is the lowest in the history of our army. Since January 1941 and up to now, excluding battle casualties, the death rate has been the lowest in the history of our army. During World War I, 1 patient of each 3 with meningitis died; now only 1 in 20 dies. Prompt diagnosis, efficient care and sulfonamides have made the difference. Overseas such conditions as malaria and dysentery are being fought with all that modern medicine has provided for the army medical armamentarium.

The information here made available should be comforting to the American fathers and mothers who have given their sons to the defense of our nation. It is information which should be spread widely so that it may reach the millions of homes in which it will answer questions that have been raised again and again in the family councils. Indeed, if there has been any one obvious deficiency it has been the failure of the Public Relations Division of the United States Army to provide the information that the people want regarding the health of our army, week by week, month by month. Let the people know about the hospitals that have been provided; let them hear about the quality of the physicians enrolled and the medical service that they render; tell about our magnificent record in the treatment of burns and wounds and in the control of malaria; tell of the training programs for thousands of surgical, laboratory, x-ray and other technicians. What about some of the research projects in which the Army has cooperated with the Navy and the Committee on Medical Research? The record of the U. S. Army Medical Corps is one in which we may all take pride; the public that we serve needs to hear of its accomplishments.

CHEMOTHERAPEUTIC AGENTS AND EXPERIMENTAL TUBERCULOSIS

The usefulness of chemotherapy in the treatment of some infectious diseases has strengthened the belief that chemical compounds may yet be found which will effectively combat the tubercle bacillus. The development of the sulfonamides has increased the fervor of those who seek such chemical weapons.

In 1938 sulfanilamide itself was found to exert an inhibitory effect on the development of tuberculosis in the highly susceptible guinea pig.[1] The drug did not prevent completely the growth of the bacilli, but fewer organisms and less extensive lesions were observed in the treated animals. Toxic doses of the chemical were required to achieve this result. The sulfone promin [2] has also been reported to have a notable inhibitory effect on the course of the disease in guinea pigs.[3] In the meantime a number of sulfonamides and related compounds have been studied with regard to their effect in experimental tuberculosis.

A recent report of Smith and his collaborators [4] of the National Institute of Health merits especial attention because it deals with a large number of compounds, including sulfonamides, sulfones and comparable phosphorus containing compounds, and because it serves as a progress report on the problem of chemotherapy in experimental tuberculosis. Therapeutic tests carried out by these investigators on experimental animals infected with a virulent human strain of tubercle bacilli showed a favorable effect with the three drugs diaminodiphenylsulfone, promin and sulfadiazine as regards both the survival time and the retardation of progress of the disease. The mortality of an untreated group of infected animals was 81 per cent after one hundred and seven days, while the comparable percentage mortality of animals treated with promin was 44 and of those treated with either of the other drugs was 56. Notably the extent of tuberculous involvement, as indicated by examination of several organs, was found to be much less in the animals treated with diaminodiphenylsulfone than in animals of the other groups. Indeed, many of the animals in the former group presented an uninterrupted growth curve after cessation of treatment, indicating attenuation of the tubercle bacillus or arrest of the infection. As pointed out by Smith and his co-workers, the toxicity of diaminodiphenylsulfone, which exerts its effect at 50 to 75 per cent of the lethal dose, makes it desirable to develop derivatives capable of producing the same or better effects with dosages further removed from the toxic level. Acording to these investigators promin does not fulfil this requirement but appears to be a step in the right direction. It is perhaps pertinent to mention that a phosphorylated derivative of diaminodiphenylsulfone has recently been prepared which, on the one hand, possesses only one-half to one-fifth the toxicity of the parent sulfone and, on the other hand, has a chemotherapeutic action against experimental pneumococcic infection which is superior to that of the original sulfone.[5] Whether or not this phosphorylated derivative will prove effective against experimental tuberculosis remains to be seen.

Work on the problem of chemotherapy in experimental tuberculosis is still in the early stage. The more recent attacks on the problem have, however, yielded encouraging results and further developments are awaited. It is hardly necessary to point out here that tuberculosis induced experimentally in guinea pigs is dissimilar to tuberculosis in human beings. The prog-

1. Rich, A. R., and Follis, R. H., Jr.: The Inhibitory Effect of Sulfanilamide on the Development of Experimental Tuberculosis in the Guinea Pig, Bull. Johns Hopkins Hosp. **62:** 77 (Jan.) 1938.

2. Promin is the sodium salt of P-P'-diaminodiphenylsulphone-N-N'-dextrose sulfonate.

3. Feldman, W. H.; Hinshaw, H. C., and Moses, H. E.: The Effect of Promin (Sodium Salt of P,P'Diaminodiphenylsulfone-N,N'-Dextrose Sulfonate) on Experimental Tuberculosis: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **15:** 695 (Oct. 30) 1940; **16:** 187 (March 19) 1941.

4. Smith, M. I.; Emmart, E. W., and Westfall, B. B.: The Action of Certain Sulfonamides, Sulfones and Related Phosphorus Compounds in Experimental Tuberculosis, J. Pharmacol. & Exper. Therap. **74:** 163 (Feb.) 1942.

5. Smith, M. I.; Rosenthal, S. M., and Jackson, E. L.: The Chemotherapeutic Action of a N-Phosphoryl Derivative of 4-4'-Diaminodiphenylsulfone, Pub. Health Rep. **57:** 1534 (Oct. 9) 1942.

ress of studies on the chemotherapy of tuberculosis in experimental animals is, nevertheless, of obvious importance. While the results of these investigations and the conclusions based on them cannot be directly applied to chemotherapy of tuberculosis in man, they do lead the way in the study of the latter problem.

THE NATIONAL CONFERENCE ON PLANNING FOR WAR AND POSTWAR MEDICAL SERVICES

Elsewhere in this issue (p. 769) appears an announcement of a proposed conference on the planning of war and postwar medical services, representing a unique assemblage in American medicine. For the first time a variety of organizations associated with many different aspects of medical services, including scientific advancement, personnel and supplies, are meeting to discuss jointly urgent problems which affect all. The organizations which participate in this conference, which has been called under the auspices of the Carlos Finlay Institute of the Americas, include the:

American Medical Association.
American College of Physicians.
American College of Surgeons.
American Drug Manufacturers Association.
American Hospital Association.
American Pharmaceutical Manufacturers Association.
American Pharmaceutical Association.
American Surgical Trade Association.
Wholesale Surgical Trade Association.
National Physicians Committee for Extension of Medical Service.

The program has been planned in three parts: a morning session concerned largely with epidemic disease and nutrition, an afternoon session concerned with personnel, supplies and research, and an evening program devoted to the ideals that should prevail in working out programs of interest to all the peoples of the world. The evening session has been limited to those specially invited to participate, but the morning and afternoon sessions are open to any physician who may be in New York on March 15 and who might wish to attend. Participation in discussions, however, will again be limited to those especially invited to participate in the conference. Mr. Basil O'Connor, president of the National Foundation for Infantile Paralysis, Inc., and also of the Carlos Finlay Institute of the Americas, an organization which was described in an editorial comment in THE JOURNAL on Jan. 17, 1942 (p. 230), will preside at the evening session.

Significant also in this national conference is the extent to which laymen and statesmen whose interests in medicine have been profound will give of their time and services in developing the contribution of America to the rehabilitation of a starved, disease ridden and war torn world.

Current Comment

THE RED CROSS CAMPAIGN

The Red Cross has just begun a national appeal for a special fund of $125,000,000 to take care of the unprecedented war demands on the organization. The Red Cross supplies the armed forces throughout the world with many comforts and needs not covered by regular military issue. In areas retaken from the enemy, the Red Cross must be and is prepared to supply food, clothing, medicines and other necessities to large numbers of persons, many of whom may be in a starving or otherwise desperate condition. This organization has taken over the procurement of blood for the preparation of plasma for the armed forces as well as for possible civilian disaster. All the material and personnel for these services and others as well must be ready in advance and available when needed. Physicians, more than any others perhaps, are fully aware of the vast humanitarian service of the Red Cross and can be counted on to support this campaign with all the influence as well as financial assets at their command.

EVAPORATED MILK

In recent weeks it has been difficult in some areas to purchase certain brands of evaporated milk. Both mothers and physicians have become concerned as to its availability for infant feeding. The amount of evaporated milk produced in 1942 was in excess of that produced in any previous year. The War Production Board has established a packing quota for 1943 for evaporated milk in 6 ounce and 14½ ounce cans of 90 per cent of the 1942 pack. An additional quantity will be packed in larger containers for institutional and military use. The Food Distribution Administration anticipates that sufficient supplies of evaporated milk will be assured to provide an adequate amount for the needs of children under 2 years of age. However, not all brands will be available in all localities. This situation is obviously not serious, since the composition of evaporated milk has less variation than almost any other canned food. Regulations of the Food and Drug Administration fix and establish definitions and standards of identity for evaporated milk; these became effective July 17, 1940. These regulations require a minimum of 7.9 per cent of milk fat and 25.9 per cent of total milk solids. Since most physicians are concerned as to the possibility that a high percentage of fat in a formula may produce digestive disturbances in infants, the fat content of evaporated milk is of major interest. The regulations establish a minimum, and there is little danger of a fat content much above this minimum. Since fat is the most expensive part of milk, manufacturers are not apt to leave more than the required amount in the product. Consideration should be given of course as to whether or not the milk is irradiated or fortified with vitamin D and to the extent of such fortification so that the milk may be supplemented with this vitamin if necessary. Physi-

cians can do a real service to their patients and their country by explaining to mothers the nature of various brands of evaporated milk, the possible use of other brands for feeding infants, if the one to which they have been accustomed is unavailable, and the special character of irradiated as contrasted with nonirradiated evaporated milk.

MENTAL SYMPTOMS FOLLOWING THE USE OF ATABRINE

The appearance of mental symptoms during or following the administration of atabrine in curative dosage has been reported by many observers. Conoley working in Perak, one of the Federated Malay States, first drew attention to the restlessness and excitement sometimes associated with the taking of atabrine. Other observers in Ceylon, India and Malaya have reported that mental symptoms are noted more commonly in patients treated with atabrine than with those on treatment with quinine. Many of these reports are summarized by J. W. Field in Bulletin 2 of 1938 from the Institute for Medical Research, Federated Malay States. He says that there is a fairly characteristic clinical course of events. Toward the end of the usual five to eight day course of oral atabrine, or perhaps a few days after treatment has been finished, the patient begins to behave strangely, becoming more or less excited, voluble and confused, or occasionally maniacal. He is mentally disturbed for about a week and gradually returns to normal without special treatment. This clinical picture, or atabrine psychosis, appeared in 13 cases among 700 treated during one period in Ceylon, 6 cases among many thousands treated in Kuala Lumpur and 4 cases in approximately 9,000 treatments in Malaya. Field concludes that the incidence of atabrine psychosis may tentatively be placed at less than one in a thousand cases treated. The incidence of mental symptoms during or subsequent to the administration of atabrine in the Western Hemisphere appears to have been at least equally small. There have been no reports of mental symptoms as a result of the administration of atabrine in prophylactic dosage. Confusional psychoses sometimes occur as a direct result of malarial infection, and some patients under treatment for malaria may have preexisting mental abnormality. Therefore it should not be assumed that every mental aberration following treatment with atabrine is necessarily due to atabrine. Atabrine is used extensively by the United States Army. Circular Letter 22, Office of the Surgeon General, War Department, Washington, D. C., Jan. 16, 1943, outlines the following optional methods of treatment for uncomplicated malaria:

1. Combined QAP treatment (method of choice).

(*a*) Quinine sulfate 0.64 Gm. (10 grains) three times daily after meals for two or three days or until pyrexia is controlled. Then give

(*b*) Atabrine 0.1 Gm. (1½ grains) three times daily after meals for five days. Then after two days without antimalarial medication give

(*c*) Plasmochin 0.01 Gm. (3/20 grain) three times daily after meals for five days, except for the debilitated patient, who should receive only two doses daily. (Discontinue if toxic symptoms occur. Never give atabrine and plasmochin concurrently.)

2. Atabrine-plasmochin treatment. (May be used for simple Plasmodium vivax infections and in other infections when no quinine is available.)

(*a*) Atabrine as described for seven days. Then after two days without antimalarial medication, give plasmochin 0.01 Gm. three times daily for five days, as described.

3. Quinine-plasmochin treatment. (Method when no atabrine is available.)

(*a*) Quinine sulfate as described for seven days, during the last five of which accompany each dose of quinine with plasmochin 0.01 Gm. three times daily.

NOTE.—Quinine sulfate tablets are more quickly effective if dissolved before being taken. Ten grains of quinine sulfate may be dissolved in 1 ounce of water which has been acidified by the addition of 10 minims of diluted sulfuric or hydrochloric acid (U. S. P.) or 2 Gm. (30 grains) of citric acid.

The same circular letter outlines as drug prophylaxis or suppressive treatment of malaria the following methods:

Atabrine in doses of 0.4 Gm. a week is recommended as the standard suppressive treatment of quinine daily. The atabrine should be taken 0.1 Gm. twice a day on two nonsuccessive days a week, with water and immediately after meals. The prophylactic dosage of quinine is 5 to 10 grains daily after the evening meal. Under present conditions quinine prophylaxis is to be used only if a man cannot tolerate atabrine.

ROLE OF AMINO ACIDS IN HUMAN NUTRITION

Present knowledge of the role of the various amino acids in nutrition is based in large part on observations on the white rat.[1] As one of a series of studies designed to determine the amino acid requirements of the human species, Rose and his colleagues[2] employed two healthy young men to serve as the subjects for preliminary tests. They found that nitrogen equilibrium in these subjects could be readily maintained by diets containing only ten amino acids. This fact demonstrates that the twelve acids previously shown to be dispensable for rats and dogs are also nonessential for man. At the expiration of the "fore period" of eight days during which these preliminary tests were made, valine was removed from the diet and the other amino acids were increased to provide a sufficient nitrogen content. The effects of this change were profound: immediately each of the two subjects manifested a negative nitrogen balance. On the fourth day the nitrogen output exceeded the intake by 2.19 and 2.91 Gm. respectively. Valine was then returned to the food and was followed quickly by the reestablishment of positive nitrogen balances. After six days on the complete diets, methionine was excluded from the food for a period of six days. Again the subjects lost more nitrogen than was ingested, although the negative balances were not so large as after valine deprivation. Immediately after the readministration of methionine, positive balances were restored. These observations demonstrate that the amino acids valine and methionine are indispensable dietary components for man; deficiencies of these amino acids create additional "deficiency diseases."

1. Lewis, H. B.: Proteins in Nutrition (Handbook of Nutrition: II), J. A. M. A. **120:** 198 (Sept. 19) 1942.
2. Rose, W. C.; Haines, W. J., and Johnson, J. E.: The Role of the Amino Acids in Human Nutrition, J. Biol. Chem. **146:** 683 (Dec.) 1942.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

SCIENTIFIC WORK IN LENINGRAD

PROF. K. KERCHEEV
Supplied by Soviet Scientists' Antifascist Committee

A rather large volume entitled "Works of the Institute for Advanced Training of Medical Practitioners" has just been published. The volume deals with sixty-eight researches carried out during the first year of the war. In September 1941 the battle front was approaching the gates of Leningrad. The streets, houses and hospitals were being bombed and shelled; the city's food supply was cut off by blockade; the hospitals were deprived of electricity, dressings, equipment and medicines, but still the city did not surrender. In spite of incessant air attacks the doctors continued to treat the sick and the wounded and at the same time made numerous attempts to discover new medicines to replace those usually employed but then unobtainable.

The problem of healing wounds was the chief concern of the medical men in Leningrad. The members of the institute, among them the surgeon N. Petrov, introduced various new methods for the treatment of wounds; they gave considerable attention to a study of roentgenographic methods of locating shell and bomb fragments, and bullets lodged in the bodies of the wounded. A number of research projects were carried on in connection with serious wounds of the face and jaws. By discovering methods of healing such wounds, Leningrad physicians saved the lives of thousands of fighters. The cure of scurvy and other hypovitaminoses due to the scarcity of food was another subject taken up by the institute.

When motor transportation was established during the winter of 1941-1942 across Lake Ladoga and supplies of food were delivered to the city of Leningrad it was possible in many cases, with the help of physicians, to relieve the effects of undernourishment. The cure of frostbite, the restoration of peripheral nerves and other problems in neurosurgery were studied by Leningrad physicians to find better ways for saving the lives of the fighters. "The interdependence of science and practice has never been felt to such an extent as during the trying months of 1941-1942" say the authors of this volume. The suggestions of doctors were immediately put into effect and served as a "stimulus to continue and widen the field of research." The efforts of these sixty-eight scientific research workers of Leningrad Institute represent heroic exploits carried out under harrowing conditions in a besieged city within range of the enemy guns. These reports prove that it is possible to continue scientific work under the most difficult conditions if the research is of sufficient importance to one's home land and vital to the needs of the army.

ARMY

CLASS OF MEDICAL INSPECTORS

A class composed of forty-two officers of the medical corps graduated at the Medical Field Service School at Carlisle Barracks, Pa., February 6, after a month's training in the course for medical inspectors, whose duties are to supervise sanitation and medical preventive measures in army camps and to make recommendations for the correction of insanitary conditions. Twenty-five members of this class had previously graduated at Carlisle Barracks from the basic courses for officers. Another class of medical inspectors, numbering about fifty medical officers, started on February 15.

MAJOR FLICKINGER AWARDED DISTINGUISHED FLYING CROSS

Major Don D. Flickinger, a graduate of Stanford University Medical School, was awarded the Distinguished Flying Cross in 1941 for his work as flight surgeon on the pioneer trip of a squadron of B17's to the Philippines. Major Flickinger has now returned from the Pacific island theater and has been appointed flight surgeon at the Mather Field, Sacramento, an advanced flying and navigation school. He has developed a rescue method for pilots forced down at sea whereby they become visible for long distances when they land in the water. Major Flickinger spent many hours in the water in developing this device.

CAPTAIN GAMSO AWARDED SILVER STAR

The War Department announced on February 14 the award of the Silver Star for gallantry in action in New Guinea to Capt. Rafael R. Gamso of Brooklyn. Captain Gamso attended the public schools of Dallas, Texas, graduated in medicine at Baylor University College of Medicine in 1936 and interned at Cumberland Hospital, Brooklyn. He went into the service on Jan. 29, 1941 and went overseas on April 1, 1942. Dr. Gamso is 31 years of age.

DR. SUTTER CITED FOR BRAVERY

Dr. LeRoy M. Sutter of Orlando, Fla., has been cited in orders of commendation for bravery under fire and for service beyond the call of duty in North Africa, the newspapers have reported. Prior to entering the Army in the spring of 1942, Dr. Sutter was on the staff of the Florida Sanitarium and Hospital in Orlando.

DOCTORS IN KHAKI

Camera men, technicians and stage director Herman Shumlin arrived at the Medical Field Service School, Carlisle Barracks, Pa., February 13, to begin the production of a movie entitled "Doctors in Khaki" for the Office of War Information for release to civilian audiences. The script, which was prepared by the well known team Mr. and Mrs. Albert Hackett, deals

with the advanced training methods developed at Carlisle Barracks for adapting the talent of medical men to combat duty. The cast will comprise the officers actually on duty at Carlisle Barracks and the officers attending classes there. Thus medical officers from all parts of the country may be seen in the picture at work preparing to save lives on far flung battle fields. The picture, which has been designed to show the training of the nation's doctors of medicine for field duty, will follow the home town physician throughout his period of study at the field service school. It will be a public feature short, released soon. Mr. Shumlin and Mr. and Mrs. Hackett are giving their time without pay in the interest of the war effort.

ARMY PERSONALS

Lieut. Col. George H. Ham of Culver City, Calif., has been appointed surgeon at the Army Air Corps Base, Key Field, Miss. Lieutenant Colonel Ham in 1930 went in training at the School of Aviation Medicine at Brookfield, Texas, then returned to the civil practice of his profession in Culver City until Dec. 15, 1939, when he was called to active duty and assigned to March Field, Calif.; since then he has served also at Glendale and at Mather Field, Calif., where he organized a 200 bed hospital, and as the surgeon of the Ferry Command with headquarters in Washington, D. C.

NAVY

PROMOTIONS FOR NAVY NURSES

Recent regulations authorized the promotion of Miss Sue S. Dauser, superintendent of the Navy Nurse Corps, to the relative rank of captain and authorized higher relative ranks for two assistant superintendents and four directors of the Nurse Corps, which now comprises 3,200 nurses. Miss Dauser, who has just been reappointed for a second four year term as superintendent of the Navy Nurse Corps, has been in the naval service since November 1917.

The two assistant superintendents of nurses who were promoted from the relative rank of lieutenant to that of commander are Loretta Lambert of Claysville, Pa., and Mary D. Towse of Pittsburgh, and the four directors promoted from lieutenant to lieutenant commander are Helen M. Bunte of McSherrytown, Pa., Elizabeth M. O'Brien of San Francisco, Myrtle R. Carver of Raleigh, N. C., and Anna G. Keating of Philadelphia. A number of other nurses were promoted from the relative rank of lieutenant (j. g.) to that of lieutenant.

KITS FOR SUBMARINE CHASERS

The Medical and Surgical Relief Committee of America, 420 Lexington Avenue, New York City, shipped on February 5 thirteen special portable emergency medical kits to a submarine chaser training center in the South and announced a drive for $25,000 to furnish similar medical kits to numerous submarine chasers in the U. S. Navy. The kits, made of fiber board with metal edges, will fit in a square foot of space. The kits thus furnished contained tourniquet, bandages, forceps, scalpel, gauze pads and ointments and medicines for the emergency treatment of burns and other injuries. In view of their size, submarine chasers are not usually staffed by medical officers.

CIVILIAN DEFENSE

ORGANIZATION OF STATE GAS SPECIALIST SCHOOLS

The Office of Civilian Defense, Washington, D. C., issued on February 9 Operations Letter No. 109, which reads as follows:

The training of gas officers and gas reconnaissance agents, as set forth in Operations Letter No. 91, requires the establishment of state gas specialist schools at universities or technical schools to supplement the gas specialist courses given at War Department civilian protection schools. Most gas reconnaissance officers and many senior gas officers will be unable to attend War Department civilian protection schools because of the limited enrolment of these schools and the time and expense involved in attendance.

It is recommended that state schools for gas specialists be established now in regions I, II, III and IX and later in the other regions. The regional sanitary engineer and gas officer should consult with the state director or coordinator of Civilian Defense and the state gas consultant in selecting the schools which will be asked to cooperate in establishing the gas specialist courses. Availability of rooming and feeding facilities for students should be considered.

The selected schools should be asked to provide teaching personnel for technical subjects, classrooms and laboratory facilities. The state gas consultant should be responsible for (1) arranging schedules of instruction with the school authorities, (2) arranging all field administrative matters such as recruiting students and arranging for demonstrations, (3) giving the instruction on organization of the state gas program.

Sanitary engineers and gas officers in these regions should arrange for the attendance at War Department civilian protection schools of one or two representatives of each of the selected universities. Candidates should be members of the faculty who are willing to assist the state defense council in organizing the course and in providing the instruction.

Tentative plans for the state gas specialist schools call for a three day course with emphasis on gas identification and reconnaissance. The gas protection section of the medical division will assist in arranging the procurement of equipment for demonstration purposes. Whenever possible, arrangements will be made for the attendance of a small military unit to demonstrate materials which cannot be placed in the hands of civilian instructors. A course outline and instructor's manual are being prepared for use in these schools.

CIVILIAN DEFENSE PERSONALS

Dr. Jack Masur, executive director of Lebanon Hospital, New York, has been commissioned past assistant surgeon in the U. S. Public Health Service and assigned to the Medical Division of the Office of Civilian Defense as hospital administration specialist to succeed Mr. Henry N. Hooper, who resigned last October to enter military service. Dr. Masur graduated from Cornell University Medical College, New York, served an internship at Bellevue Hospital and had a residency at Montefiore Hospital, New York, from which hospital he was a traveling fellow to the medical service of Prof. I. Snapper in Amsterdam, Netherlands.

Dr. Abraham N. Franzblau, professor of religious education and pastoral psychology at Hebrew Union College, Cincinnati, has been commissioned a past assistant surgeon in the U. S. Public Health Service and has been appointed to the Medical Division of the Office of Civilian Defense, Washington, D. C. Dr. Franzblau received his Ph.D. in 1934 in psychology and education and graduated from the University of Cincinnati College of Medicine in 1937, since which time he has been a fellow in research on diabetes and myasthenia gravis at the Jewish Hospital in Cincinnati.

Dr. Dudley A. Reekie, Boston, regional medical officer of the first civilian defense region, has been assigned acting chief of the Field Casualty Section of the Office of Civilian Defense in the absence of Dr. Leonard A. Scheele, who is assigned to special duty. Dr. A. William Reggio, Boston, state chief of Emergency Medical Service, is acting regional medical officer.

Dr. Lloyd H. Gaston, Baltimore, assistant regional medical officer in the third civilian defense region, has been transferred to Chicago to become assistant regional medical officer, associated with Dr. John S. Coulter, regional medical officer for the sixth region.

MISCELLANEOUS

VICTORY STUDENT NURSE CORPS PROPOSED

Mr. Paul V. McNutt, federal security administrator, is considering a proposal by the Health and Medical Committee of the Office of Defense Health and Welfare Services intended to help meet the critical shortage of nurses. The proposal includes provisions for stipends for student nurses, the use of a portion of the senior students in government and military hospitals, and distinct insignia for the corps; also the condensing of the training period for student nurses from thirty-six to thirty or twenty-four months. Maintenance would be provided throughout the training period and, on graduation, nurses either would enter the armed forces with the rank and pay of second lieutenant or ensign or be assigned to governmental or civilian nursing services essential to the war effort. Any student enrolled in a participating school of nursing after Jan. 1, 1941 would be eligible to volunteer for the Victory Student Nurse Corps. In connection with this proposal, Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service, said that future quotas of the army and navy cannot be made from the current nurse supply without a threatened collapse of nursing care for the civilian population.

PERUVIAN PHYSICIAN VISITS PLASMA LABORATORIES

Dr. Jorge Avendano, director of the clinical laboratories of the Hospital de Obreros, Lima, Peru, is visiting a group of Eastern hospitals under the auspices of the Office of the Coordinator of Inter-American Affairs and the Office of Civilian Defense to study the organization of blood and plasma banks and the preparation of both liquid and dried plasma. Arrangements for Dr. Avendano's visit to the United States were made through the Division of Health and Sanitation of the Coordinator's Office, and his itinerary of hospitals was arranged by the Medical Division, Office of Civilian Defense. The Medical Division, in cooperation with the U. S. Public Health Service, is assisting about one hundred and fifty hospitals in target areas to establish blood and plasma banks in order that adequate reserves of plasma may be available for the treatment of casualties caused by enemy action or any major wartime disaster. Dr. Avendano is spending two weeks at the Bryn Mawr Hospital, Bryn Mawr, Pa., and several days each at Albany Hospital, Albany, N. Y.; Strong Memorial Hospital, Rochester, N. Y., and Syracuse University Hospital, Syracuse, N. Y.

MILITARY CROSS AWARDED TO PHYSICIAN PARACHUTIST

Lieut. Charles Granville Rob of the Royal Air Force medical corps has been awarded the Military Cross, according to a dispatch from London, February 11. He is said to be the first "parachuting doctor" to gain a military award. After a flight of 350 miles and a parachute drop he performed one hundred and forty surgical operations, under extremely difficult conditions and bombings in Tunisia. After performing many operations in one day, he is said to have given a pint of his own blood when the supplies of blood ran short.

PERSONALS

Miss Marion W. Sheahan of Albany, N. Y., director of the Division of Public Health Nursing of the New York State Department of Health, has been appointed chairman of the Subcommittee on Nursing, Health and Medical Committee, Office of Defense Health and Welfare Services, Washington, D. C. The purpose of this subcommittee is to make over-all studies of nursing needs and recommend methods of meeting them, and to coordinate all phases of the nation's wartime nursing problems. Miss Jean Henderson, public relations consultant of the Florida State Department of Health, has been appointed information consultant to the Subcommittee on Nursing of the Health and Medical Committee, Office of Defense Health and Welfare Services, Washington, D. C.

PUBLIC HEALTH UNDER HITLER

NPD of Dec. 14, 1942 states that following an invitation of the reich minister for the occupied eastern territories Dr. Conti, the reich health leader, is spending several days in the reich commissariat Ostland. Dr. Conti intends to visit the authorities and institutions of the German health services with the reich commissioner and the commissioner generals in Riga, Tallinn and Kaunas, so that he can acquaint himself personally and on the spot with the work of reconstruction carried out so far.

In order to ensure supplies of medicines and dressings for the Ostland, the "Pharm-Ost-Ltd." has been set up in connection with the reich ministry for the occupied eastern territories.

An order made by the reich commissar for the Ostland announces the establishment of "chambers of health" in Estonia, Latvia and Lithuania. These chambers of health unite the following professions of the health services: physicians and their assistants, dentists and their assistants, pharmacists and their assistants, midwives and nurses.

NDZ of Dec. 3, 1942 says that cancer is one of the diseases which, next to tuberculosis, is not yet being properly dealt with. An average of 150,000 people per annum die of cancer in Germany and 500,000 people suffer from cancer. The fight against cancer has now been put on a new basis by the formation of a reich committee for combating cancer. In the periodical *Gesundheitsführung* the deputy president of the committee, Dr. Ramm, describes the task of the committee as consisting in issuing directives for the fight against cancer and for its prevention, diagnosis and cure, holding a census of the number of sufferers from cancer and investigating the course of the disease, promoting the specialized training of doctors and finally conducting a large scale campaign against public ignorance.

It is intended to set up an advice center in every kreis of the reich. All facilities for diagnosis and cure are to be available in every gau. Parallel with the efforts to insure an early diagnosis of the disease, the reich health directorate will take steps to improve preventive measures. These will have to extend, for instance, to matrimonial advice, to regulating the manner of living and insuring a natural diet. In addition the writer demands that all women above the age of 30 and men roughly from the age of 40 to 45 should periodically be examined for prophylactic purposes. He does not, however, advocate that this examination should be compulsory but expects that by appealing to the sense of duty of the more enlightened parts of the population it will be possible to carry out these measures on a voluntary basis.

The *Frankfurter Zeitung* of Dec. 2, 1942 reports a decree by Koch, the gauleiter of East Prussia, saying that the schools in East Prussia must devote at least two lessons a month to teaching their pupils personal hygiene and decent manners. Koch orders that at least once a week every form master must ascertain whether every child has a clean handkerchief, whether the hands, face and clothes are clean, the hair cut and the boots kept in proper condition. He must pay special attention to cleanliness of the hands, ears and scalp. He must examine whether the child's clothes are whole, clean and properly aired. He must examine the condition of the children's schoolbooks and at the same time instruct them in the principles of personal hygiene. He must constantly watch the children's state of health and immediately report anything unusual to the parents and the school doctor. In particular he must see to it that the children do not run about in damp clothes before lessons if the weather is bad but must make them change their boots and order them to exercise to get warm. He must make sure that the classrooms are properly aired and that the children regularly get an uncooked breakfast.

According to *Svenska Dagbladet*, Stockholm, January 14, the rumors which circulated in Norway about the death of Germans during a march across the mountains has been confirmed. The German troops, consisting of some infantry and two bicycle companies, were traveling 150 kilometers across Saltfjellet in Nordland County to Fauske. Because of the snow and cold weather the soldiers covered only 30 kilometers on the first day and spent the night in cold barracks. The men were insufficiently clad, and 6 froze to death and about 100 were frostbitten.

ORGANIZATION SECTION

OFFICIAL NOTES

NATIONAL CONFERENCE ON PLANNING POSTWAR MEDICAL SERVICES

On March 15 at the Waldorf-Astoria, New York, will be held the National Conference on Planning for War and Postwar Medical Services, under the auspices of the Carlos Finlay Institute of the Americas. Cooperating in holding the conference are the American Medical Association, the American College of Physicians, the American College of Surgeons, the American Drug Manufacturers Association, the American Hospital Association, the American Pharmaceutical Manufacturers Association, the American Pharmaceutical Association, the American Surgical Trade Association, the Wholesale Surgical Trade Association and the National Physicians Committee for the Extension of Medical Service.

The announcement of the conference explains that "There is an urgent need to mobilize the leaders of the medical profession and of the supporting industries for planning of postwar medical services."

The Carlos Finlay Institute of the Americas was organized a year ago[1] in Havana, Cuba, to foster scientific interchange and good will among the medical professions of the Latin American countries. Mr. Basil O'Connor, New York, president of the National Foundation for Infantile Paralysis, is president of the institute. Directors are Dr. Morris Fishbein; Dr. Morton Kahn; Lieut. Col. Thomas Mackie, M. C., U. S. Army; Dr. Edgar Mayer; Mr. O'Connor, and Dr. James E. Paullin. The institute was incorporated in New York state in December 1942. Representing the cooperating organizations in arranging the conference are one hundred and seventeen leaders in medical and allied fields.

The morning and afternoon sessions of the conference will be open to all interested physicians, but the evening session will be limited to an invitation list. All sessions will be held at the Waldorf-Astoria.

Presiding at the morning session, which will start at 10 o'clock, will be Dr. James E. Paullin, Atlanta, Ga., president of the American College of Physicians and President-Elect of the American Medical Association. Speakers and their subjects will be: Lieutenant Colonel Mackie, executive officer, Tropical and Military Medicine, Army Medical School, Washington, D. C., "War and the Migration of Tropical Diseases"; Dr. Thomas Francis Jr., professor, Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Mich., "Epidemiology of Influenza"; Dr. Lowell T. Coggeshall, University of Michigan School of Public Health, "Malaria—A World Menace," and Dr. John B. Youmans, associate professor of medicine, Vanderbilt University School of Medicine, Nashville, Tenn., "Nutritional Diseases as a Postwar Problem."

At the afternoon session, which will convene at 2:30, Brig. Gen. Fred Rankin, M. C., U. S. Army, President of the American Medical Association, will preside. Speakers and their subjects will be: Edward C. Elliott, Ph.D., LL.D., president, Purdue University, member War Manpower Commission, Washington, D. C., "Postwar Needs for Medical and Other Trained Personnel"; Col. C. F. Shook, M. C., U. S. Army, Washington, D. C., "Postwar Channeling of Drugs and Medical Supplies," and A. R. Dochez, Rockefeller Institute for Medical Research, "Trends in Scientific Research."

The evening session will be a dinner meeting, starting at 7 o'clock. Mr. John G. Searle, president of the American Drug Manufacturers Association, will introduce Mr. O'Connor, who will preside as toastmaster.

Mr. Nelson A. Rockefeller, coordinator of Inter-American Affairs, Washington, D. C., will speak on "The Health Problems of the Americas."

Mr. Frederick P. Keppel, director, Equitable Life Assurance Society of the United States and of the U. S. Guaranty Trust Company, New York, will speak on "Health—A World Problem."

Mr. Norman Davis of the American Red Cross, Washington, D. C., will tell of "The Place of the American Red Cross in Medical Rehabilitation."

Dr. Fishbein, Editor of THE JOURNAL, will speak on "American Medicine's Contribution to the Postwar World."

1. Finlay Institute of the Americas, J. A. M. A. **118:** 230 (Jan. 17) 1942.

REPORT OF MEETINGS OF THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS, HELD IN CHICAGO, FEB. 13 AND 14, 1943

The Liaison Committee of the Council on Medical Education and Hospitals and the Association of American Medical Colleges met Saturday evening, February 13, at the Palmer House in Chicago.

The Council approved the basic pattern of the army specialized training program for premedical students as presented by Col. F. M. Fitts of the Army Specialized Training Division, Headquarters, Services of Supply, Washington, D. C.

Inter-American relationships in the field of graduate medical education were discussed.

In view of the war demand, the Council withdrew objection to medical schools recorded as on a probationary status on the list of approved medical schools maintained by the Council adopting accelerated programs. This action was taken with the understanding that the responsibility for such programs and the maintenance of standards should be definitely accepted by these schools.

The Council considered reports on eight medical schools visited by the Secretary.

The probationary status of the University of Georgia School of Medicine on the list of approved medical schools maintained by the Council was removed, thus restoring this school to unconditioned approval.

Consideration was given to suggested programs for the development of two schools of the basic medical sciences into complete medical schools.

The Council appointed a committee to confer with representatives of the American Hospital Association and the Association of American Medical Colleges in regard to the general problem of hospital internships.

Attention was given to the problem of the Council meeting its responsibilities during the war period with a more or less depleted staff.

The following internships and residencies were approved by the Council:

Hospitals Approved for Internships

San Joaquin General Hospital, French Camp, Calif.
St. Joseph's Hospital, Joliet, Ill.
Jennie Edmundson Memorial Hospital, Council Bluffs, Iowa.
Nazareth Hospital, Philadelphia.
Alexandria Hospital, Alexandria, Va.

Approved Residencies

Medicine
St. John's Hospital, St. Louis.
Mixed
Mercy Hospital, Hamilton, Ohio.
All Saints Episcopal Hospital, Forth Worth, Texas.
Neurosurgery
University of Chicago Clinics.
Pediatrics
General Hospital of Fresno County, Fresno, Calif.
Surgery
St. Francis Hospital, Wichita, Kan.
St. John's Hospital, St. Louis.
Bronx Hospital, New York City.
St. Paul's Hospital, Dallas, Texas.
Mary Fletcher Hospital, Burlington, Vt.
Tuberculosis
Hospital for Incipient Tuberculosis, Ray Brook, N. Y.
Schenectady County Tuberculosis Hospital, Schenectady, N. Y. (Glenridge Sanatorium)

Additional residencies were reviewed by the Council, but final action is being held in abeyance pending approval by the

respective specialty boards with which the Council has a program for concurrent approval of residencies.

The following technical schools were approved by the Council:

Schools for Clinical Laboratory Technicians Approved

St. Joseph's Hospital, Denver.
New Britain General Hospital, New Britain, Conn.
Waterbury Hospital, Waterbury, Conn.
Methodist Hospital of Central Illinois, Peoria, Ill.
Rockford Memorial Hospital, Rockford, Ill.
St. Anthony's Hospital, Rockford, Ill.
Maine General Hospital, Portland, Maine.
St. Joseph's Hospital, Baltimore.
Taunton State Hospital, Taunton, Mass.
Tewksbury State Hospital and Infirmary, Tewksbury, Mass.
Port Huron Hospital, Port Huron, Mich.
Northwestern Hospital, Minneapolis.
Bishop Clarkson Memorial Hospital, Omaha.
Newark Beth Israel Hospital, Newark, N. J.
Prospect Heights Hospital, Brooklyn.
Meadowbrook Hospital, Hempstead, N. Y.
Beth Israel Hospital, New York.
St. Luke's Hospital, New York.
Grasslands Hospital, Valhalla, N. Y.
St. Luke's Hospital, Bethlehem, Pa.
Williamsport Hospital, Williamsport, Pa.
Mount Sinai Hospital, Milwaukee.

School for Physical Therapy Technicians Approved

Graduate Hospital of the University of Pennsylvania, Philadelphia.

School for Occupational Therapy Technicans Approved

New York University, New York.

Plans were formulated for revising the "Essentials of an Acceptable School for Physical Therapy Technicians" and the "Essentials of an Acceptable School of Occupational Therapy," as well as the preparation of minimum "Essentials of an Acceptable School for Medical Record Librarians."

Consideration was given to a progress report of the Council's cooperation with the American Medical Association's Committee on Health Resorts involving the inspection of health resorts by the staff of the Council.

Other items were discussed or are under consideration.

The Council met with the Advisory Board for Medical Specialties on Sunday evening, February 14.

H. G. WEISKOTTEN, Secretary.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—S. 739 and H. R. 1912 have been respectively reported to the Senate and House with recommendation that they pass. These bills are identical in phraseology and provide that during the present war and for six months thereafter personnel of all components of the Army of the United States may be detailed as students at technical, professional and other educational institutions or as students, observers or investigators at industrial plants, hospitals and other places. H. R. 1975 has passed the House, making certain deficiency appropriations. The House Committee on Appropriations refused to include in the bill an authorization of $1,200,000 for the Children's Bureau to utilize in making grants for emergency maternity and infant care for wives and infants of certain enlisted men. An effort to have inserted in the bill this authorization on the floor of the House was unsuccessful.

Bills Introduced.—S. J. Res. 34, introduced, by request, by Senator Russell, Georgia, proposes to establish the first week in October of each year as "National Employ the Physically Handicapped Week." H. R. 1879, introduced by Representative Bennett, Michigan, proposes a federal appropriation of $700,000 to construct a veterans' hospital in the Upper Peninsula of Michigan to accommodate 150 bed patients. S. 785, introduced by Senator Walsh, Massachusetts, and H. R. 1936, introduced by Representative Maas, Minnesota, would authorize an appropriation of $2,000,000 to provide for the expansion of facilities for hospitalization of dependents of Naval and Marine Corps personnel. H. R. 1956, introduced by Representative Sadowski, Michigan, provides that every person in the military or naval forces of the United States, including the Women's Army Auxiliary Corps, the Women's Reserve of the Naval Reserve, the Women's Reserve of the Coast Guard and the Women's Reserve of the Marine Corps, shall be exempt from all taxes imposed by the United States on income. S. 778, introduced by Senator Stewart, Tennessee, proposes to authorize an appropriation of such sums as may be necessary to enable each state to furnish financial assistance to needy individuals who are permanently and totally disabled. H. R. 1990, introduced by Representative Hoch, Pennsylvania, proposes to establish a Chiropody Corps in the Medical Corps of the Army and to establish within the Medical Corps a Chiropody Reserve Corps in accordance with the provisions of the National Defense Act with rank, promotion, pay and allowance equivalent to that of the Dental Corps.

STATE MEDICAL LEGISLATION

Arizona

Bill Introduced.—H. 165, to amend the workmen's compensation act, proposes to authorize an injured employee to elect to be attended by a licensed chiropractor and thereafter to be entitled to the benefits of the workmen's compensation act to the same extent as if attended by a licensed practitioner of medicine and surgery.

Arkansas

Bill Introduced.—S. 162, to amend the medical practice act, proposes to repeal the provisions providing for the annual registration of resident and nonresident practitioners holding licenses issued by the State Medical Board of the Arkansas Medical Society.

Colorado

Bills Introduced.—H. 112 proposes to exempt physicians from annually registering their certificates during the term of active duty with the Army, Navy, Marine Corps, Coast Guard, State Militia, Red Cross or in the military service of any of the Allies of the United States. H. 199, to amend the chiropractic law, proposes to require chiropractors, at the time of the annual renewal of their licenses, to present proof that they have attended at least three days of a scientific clinic, forum or educational study approved by the Colorado state board of chiropractic examiners.

Delaware

Bills Passed.—S. 38 passed the senate, February 15. It proposes to authorize the medical council of Delaware to issue temporary emergency certificates to physicians licensed outside the state. S. 41 passed the senate, February 16. To amend the medical practice act, it proposes to exempt therefrom the treatment of human ills by prayer or spiritual means in accordance with the tenets of any well recognized religious denomination.

Georgia

Bill Introduced.—S. 85, to amend the uniform narcotic act, proposes, among other things, to exempt from the operation of the act the administering, dispensing and selling at retail of certain attenuated narcotic preparations.

Bill Passed.—H. 136 passed the house, February 22. It proposes to require all licensed physicians attending a pregnant woman to take a sample of blood within thirty days of the first examination and to submit such sample to an approved laboratory for a serologic test for syphilis.

Indiana

Bill Passed.—S. 135 passed the senate, February 12. It proposes to prohibit school authorities from employing food handlers who are addicted to drugs or who have tuberculosis or syphilis in an infectious stage and to require all school employees to undergo a physical examination for tuberculosis at least once every three years by a duly licensed doctor of medicine.

Iowa

Bills Introduced.—S. 291, to amend the workmen's compensation act, proposes to provide for the payment of workmen's compensation benefits for any disability due to a disease con-

tracted by the employee in connection with the work under the employment. S. 295 proposes that, in the management of a hospital established by a county, city or town with funds received by gifts, no discrimination shall be made against the practitioners of any school of medicine recognized by the laws of the state, each patient shall have the right to employ at his expense any physician of his own choice, any such physician shall have the exclusive charge of the care and treatment of the patient in such hospital, and the attending nurses shall be subject to the direction of such physician. S. 299, to amend the law relating to the licensing of maternity hospitals, proposes to redefine "maternity hospital" so as to include any general hospital.

Bill Passed.—S. 82 passed the senate, February 18. To amend the income tax law, it proposes to authorize taxpayers to deduct expenses for the medical care of the taxpayer, and the term "medical care" is defined as amounts paid for the diagnosis, cure, mitigation, treatment or prevention of disease, or for the purpose of affecting any structure or function of the body. A senate amendment of February 18 proposed to allow also a deduction for treatment or nursing as prescribed by a well recognized church or religious denomination in a hospital or sanatorium conducted by such church or denomination.

Kansas

Bills Introduced.—S. 227 proposes to provide workmen's compensation for certain occupational disease. H. 91, previously referred to, was so amended in the house on February 11 as to authorize the state board of osteopathic examination and registration to grant temporary licenses to osteopaths licensed outside the state during the present war emergency.

Maryland

Bill Introduced.—H. 276 proposes to require any physician who knows, or has reason to believe or suspect, that any person under his professional care is infected with syphilis, gonorrhea or any other venereal disease to give immediate notice thereof in writing to the state board of health.

Bill Passed.—S. 84 passed the house, February 16. It proposes to amend the medical practice act by eliminating the proviso that no two courses of medical lectures shall be either begun or completed within the same calendar year. This amendment is for the purpose of enabling graduates of accelerated medical courses to obtain licensure in Maryland.

Bill Enacted.—S. 47 has become chapter 23 of the Laws of 1943. It increases from one to two dollars the fee which a physician may receive for executing a certificate under the employment law.

Massachusetts

Bills Introduced.—H. 723 proposes to require a chartered hospital to accept any patient when so requested by a physician licensed to practice medicine in the state. H. 868 proposes to require an operating surgeon, after the removal of any limb or organ, to deliver a written statement of explanation to the patient or the patient's husband, wife or relatives advising the nature of the operation which he performed and giving reasons for considering such operation necessary. H. 869 proposes to require every qualified physician to submit, at least twice a year, to a blood test for syphilis and gonorrhea.

Bill Passed.—H. 1013 passed the house on February 16 and the senate on February 23. It proposes to add the requirement that physicians report all cases of wounds from a BB gun to the commissioner of public safety and to the police authorities.

Minnesota

Bill Passed.—H. 273 passed the house, February 11. It proposes that physicians in the armed forces shall not be required to renew their annual licenses during the term of such service and shall be exempt from payment of all renewal fees.

Missouri

Bill Introduced.—H. 214 proposes to exempt physicians from renewing their licenses annually during the term of their military service.

Montana

Bills Passed.—S. 63 passed the senate on February 15 and the house on February 22. It proposes to authorize certain institutions of higher learning in Montana to obtain custody of unclaimed human bodies for use in the teaching and demonstration of anatomic science by professional instructors. S. 97 passed the house, February 22. It proposes to relieve physicians in the military service of the United States from paying annual license fees during the period of such service. H. 118 passed the house, February 18. To amend the medical practice act, it proposes to authorize the board of medical examiners to prescribe and enforce reciprocity requirements current with changes in standards of the practice of medicine and surgery.

Nevada

Bill Introduced.—A. 114 proposes to define the term "to practice as an osteopathic physician" to mean the right to practice the art or science of healing limited to the manipulation of the bones and by other manual manipulations intended to restore the deranged mechanism of the human body; provided that any license granted under this proposal shall not give the holder thereof the right to practice obstetrics, nor to administer or prescribe drugs or medicine of any kind, nor to perform operations in surgery by the use of the knife or other instruments.

New Hampshire

Bill Enacted.—H. 54 was approved, February 16. It provides for the establishment of a state department of health to take over the powers and duties of the state board of health.

New Jersey

Bill Introduced.—S. 72, to amend the public school law, proposes to make immunization for diphtheria a mandatory rather than optional prerequisite to attendance at school and to make it mandatory for boards of education to provide the necessary equipment to immunize pupils whose parents, in the opinion of the board, are unable to meet the necessary expense.

Bill Passed.—A. 94 passed the assembly, February 22. To amend the medical practice act, it proposes to exempt therefrom persons taking charge temporarily, on written permission of the board, of the practice of a lawfully qualified physician in the state, and further proposes conditions under which the board may grant such temporary permission.

New Mexico

Bills Introduced.—S. 101 proposes to require the county school superintendent to see that all children in his county of school age under 8 years are immunized against diphtheria. S. 160 proposes that any person having a license to practice a profession in the state shall not be prejudiced by reason of having been drafted into the armed services but shall retain such license after release from such service.

Bill Enacted.—S. 141 was approved, February 10. It provides that every physician who makes a diagnosis in or treats or prescribes for a case of venereal disease shall report such case immediately to the municipal or district health officer.

New York

Bill Introduced.—A. 880, to amend the workmen's compensation act, proposes to authorize an injured employee, when care is required for an injury to his foot, to be treated by a duly registered and licensed podiatrist of his own choosing.

Bill Enacted.—A. 377 has become chapter 12 of the Laws of 1943. It authorizes a taxpayer to deduct, for income tax purposes, expenses paid or incurred during the taxable year for medical care of himself, his spouse or his dependents. "Medical care" is defined as amounts paid or incurred for the diagnosis, cure, mitigation, treatment or prevention of disease, or for the purpose of affecting any structure or function of the body or for maternity cases (including amounts paid for accident, hospitalization or health insurance).

North Carolina

Bill Introduced.—H. 513, to amend the optometry law, proposes to authorize the state board of optometry to make use of the injunctive process in restraining the illegal practice of optometry.

Bill Enacted.—H. 110 was ratified, February 15. It authorizes state institutions for the care of the sick, feebleminded or insane to have performed on persons dying in such institutions a postmortem examination in the laboratories of incorporated medical schools, after securing the written consent of the deceased person's husband or wife or next of kin.

North Dakota

Bill Introduced.—H. 229 proposes a law for the organization and regulation of nonprofit hospital service plan corporations.

Bill Passed.—S. 57 passed the senate, February 19. It proposes the enactment of a uniform narcotic act.

Oklahoma

Bill Introduced.—S. 129 proposes to authorize a person desiring employment, who has a physical defect which would impose on his employer a further or unusual hazard, to waive such physical defect on behalf of himself or his dependents and thus to forego any right to compensation for a personal injury which might be found to be attributable in a material degree to such physical defect.

Oregon

Bill Introduced.—S. 248 proposes to require persons employed as food handlers to obtain, at six month intervals, a physician's certificate showing freedom from any infectious and contagious disease.

Bills Passed.—S. 175 passed the senate, February 16. It proposes to increase the annual registration fee from five to ten dollars for the period beginning Jan. 1, 1944. H. 350 passed the house, February 20. It proposes to authorize commissioned medical officers of the army to execute the required certificate necessary under the state premarital examination law.

Bill Enacted.—S. 91 was approved, February 19. It amends the osteopathic practice act by requiring osteopaths to register annually.

Pennsylvania

Bills Passed.—H. 235 passed the house, February 23. It proposes to authorize the state board of medical education and licensure to issue temporary certificates to physicians licensed in other states to authorize them to practice medicine and surgery in Pennsylvania for the duration of the present war and six months thereafter. H. 236 passed the house, February 23. It proposes that for the duration of the war a minimum of nine months rather than one year internship shall constitute the necessary legal training to qualify for admission to examination for a license to practice medicine.

Rhode Island

Bill Introduced.—H. 665 proposes to add rheumatic fever to the list of diseases which physicians must report to the state department of health.

South Carolina

Bill Passed.—S. 17 passed the house, February 11. It proposes to eliminate from the medical practice act the requirement that the necessary four full courses of lectures of at least twenty-six weeks each must have been given in four different calendar years. The purpose of this proposal is to enable graduates of accelerated medical courses to obtain licensure in South Carolina.

Tennessee

Bill Passed.—H. 420 passed the senate, February 9. It proposes to prohibit the sale or advertisement of articles used for the prevention of conception without a license issued by the state board of pharmacy, except that physicians and medical practitioners regularly licensed to practice medicine or osteopathy in the state of Tennessee would not be prevented from prescribing such articles.

Bills Enacted.—H. 39 has become chapter 107 of the Public Acts of 1943. It provides that hospitals and physicians called on to render first aid to persons suffering from any wound or other injury inflicted by means of a knife, pistol, gun or other deadly weapon or suffering from the effects of poison or suffocation shall report the same immediately to the chief of police. H. 129 has become chapter 49 of the Public Acts of 1943. It provides for the creation of a state board of naturopathic examiners and defines naturopathy as the prevention, diagnosis and treatment of human injuries, ailments and diseases by means of any one or more of the psychological, physical or mechanical, chemical or material, forces or agencies of nature. The act shall not be construed, however, to permit or authorize any naturopathic physician licensed thereunder to perform any surgical work other than minor matters. H. 903 has become chapter 117 of the Public Acts of 1943. It amends the workmen's compensation act to provide that an employer shall designate a group of three or more reputable physicians or surgeons from which the injured employee shall have the privilege of selecting the operating surgeon or the attending physician.

Texas

Bills Introduced.—S. 114 and H. 208 propose that the superintendent of a state hospital shall be a skilled physician authorized to practice medicine in Texas and of not less than five years' experience in the treatment of mental diseases. H. 14, to amend the marriage law, proposes to require a male applicant for a marriage license to produce a certificate from a reputable licensed physician to show that he is free from all venereal diseases. H. 65, to amend the marriage law, proposes that each applicant for a marriage license shall produce a certificate signed by a physician legally licensed to practice medicine in Texas showing such applicant to be free from syphilis and all other venereal diseases. Furthermore, the certifying physician would be required to retain in his office for a period of at least five years a detailed report of any laboratory test made.

Utah

Bills Introduced.—H. 29, previously referred to, was amended in the senate on February 16 so as to require applicants for a license to practice naturopathy to have completed at least one year of internship in a hospital accredited by the American Hospital Association. H. 160 proposes that any person with tuberculosis in a communicable form who fails to obey the tuberculosis laws or rules of the state board of health may be committed to a sanatorium on complaint by a health officer or a physician or surgeon licensed in the state of Utah.

Vermont

Bills Introduced.—S. 16 proposes to authorize the institutionalization and treatment of persons who violate the criminal laws or who are guilty of gross immoral conduct because of mental deficiency, insanity or psychopathic personality. The latter term is defined as the existence in any person of such conditions of emotional instability or impulsiveness of behavior, lack of customary standards of good judgment, or failure to appreciate the consequences of his acts, as render him irresponsible for his conduct with respect to sexual or other criminal behavior and thereby dangerous to other persons. H. 74, a substitute for H. 50, to amend the law relating to the practice of medicine and osteopathy, proposes to authorize the examining board to make rules and regulations covering requirements for admission to practice medicine and surgery and osteopathy. H. 151, to amend the premarital examination law, proposes to authorize the execution of the required certificate by an osteopath and by a member of the medical corps of the army, navy or public health service.

Bill Passed.—H. 50 passed the house, February 12. It proposes to amend the medical practice act by repealing the section setting forth the requirements for admission to practice and to substitute therefor an authorization that the board shall make rules and regulations covering requirements for admission to practice medicine and surgery.

Washington

Bills Introduced.—S. 181 proposes the creation of full time health districts within the state, provides for the establishment of district boards of health and the appointment of district health officers and prescribes their duties. S. 214 proposes to require all persons employed in the preparation, serving or handling of food to be examined by the city health officer and to obtain a certificate showing freedom from any and all communicable diseases at least once every six months. The health officer is limited to a fee of two dollars for making such examination and certificate. S. 222 proposes the creation of a state board of practical nurse examiners and defines practical nursing as the performing for compensation of such services as are necessary in the attendance on or the care of persons ill from chronic disease or convalescent, handicapped, mentally unbalanced or aged persons in homes, hospitals or institutions depending on or under the supervision of a regularly licensed and practicing physician. H. 121 proposes to exempt charitable hospitals from taxation under certain conditions. H. 245 proposes the creation of a cash sickness compensation fund and provides for the administration of such fund. H. 256 proposes to require every elementary school from the sixth grade on and every high school or junior high school to institute and maintain as a regular part of its curriculum a course of study and practice of emergency first aid methods.

Bills Passed.—S. 218 has passed the senate. It proposes to authorize the director of licenses, during the present emergency, to grant temporary certificates to practice medicine and surgery to physicians duly licensed and qualified to practice under the laws of some other state and proposes that such temporary license shall be valid from the date of issuance until the next regular examination given by the board of examiners. H. 41 passed the house, February 10. It proposes to authorize the establishment of emergency health and sanitation areas and sets forth certain regulations applicable to the state board of health in connection therewith. H. 127 passed the house, February 12. It proposes to make it unlawful for any person to maintain or operate a maternity home without a license and defines maternity home as any place where women go to be delivered of children.

West Virginia

Bills Introduced.—S. 110 and H. 181, to amend and reenact the law relating to mentally ill persons and mental defectives, propose, among other things, that the head of the newly created division of mental hygiene shall be a reputable physician and a graduate of an accredited medical school with at least five years' actual experience in the practice of his profession and at least three years' actual experience as a physician in an institution for the care and treatment of mental illness. The proposals also provide for the licensing of all private institutions for the care, custody or treatment of mentally ill or mentally defective persons. H. 264, to amend the medical practice act, proposes to exempt therefrom persons practicing Christian science.

Bills Passed.—S. 36 passed the senate, February 24. It proposes the creation of a division of cancer control in the state department of health to administer provisions relating to the diagnosis, treatment and care of persons suffering from cancer, including the conduct of an educational program, the establishment of cancer clinics in general hospitals throughout the state and the furnishing of tissue diagnostic service to all patients. S. 85 passed the senate, February 23. It proposes to authorize the board of governors of the West Virginia University to establish a four year medical course to be given either at the university or in part at other universities and medical colleges outside the state.

Wisconsin

Bill Passed.—S. 53 passed the senate, February 17. It proposes to exempt members of the armed forces from being required to maintain a license to practice any profession within the state, proposes that this license shall be suspended during the active service of such persons, and proposes that it may be renewed within six months after such persons' discharge.

Wyoming

Bills Passed.—H. 58 passed the house, February 12. It proposes to prohibit the operation of a maternity hospital without a license issued by the state board of health. H. 77 passed the house, February 12. It proposes regulations for the compulsory sterilization of inmates of certain state institutions if the inmates have been found to be insane, idiotic, imbecilic, feebleminded or epileptic and the probable potential parents of socially inadequate offspring.

Bills Enacted.—S. 2 has become chapter 7 of the Laws of 1943. It amends the premarital examination law by (1) requiring the test to be made on females as well as males and (2) authorizing the execution of the certificate by any physician duly licensed under the laws of Wyoming and engaged in practice there. H. 22 has become chapter 39 of the Laws of 1943. It amends the pharmacy law by providing that a hospital shall not be prohibited from keeping on hand and using professionally drugs, medicine or narcotics under the direction of physicians, dentists or veterinarians, even though there be no registered pharmacist present.

WOMAN'S AUXILIARY

New Jersey

A symposium on "Doctors' Wives in the War Effort and Home Community Service" made memorable the first of a new type of meeting of the Woman's Auxiliary to the Essex County Medical Society, Nov. 23, 1942, at the Academy of Medicine. The program chairman, Mrs. S. Bernard Kaplan, introduced the uniformed members of the auxiliary prominently engaged in community activities. Mrs. Henry C. Barkhorn, vice chairman of the Newark Red Cross chapter and chairman of the Woman's Division of the War Chest and Roll Call, presided. Mrs. H. Roy Van Ness discussed the many ways in which doctors' wives have aided in establishing community projects of help to the medical profession. Mrs. A. Elston Fink told how the wives of doctors at war could substitute for their absent husbands by listening to patients' woes and by entering actively in community projects. Mrs. Arnold Kallen and Mrs. Arthur Heyman, wives of two doctors who are with the Armed Forces, spoke of the spiritual satisfaction that they had found in their volunteer work as Nurses' Aides. Mrs. Asher Yguda, auxiliary president and wife of a naval officer, described life in a naval community and how she has organized the Civilian Defense of that community.

Virginia

The Norfolk auxiliary met on Dec. 2, 1942 under the presidency of Mrs. W. E. Butler. Dr. A. Brownley Hodges, Civilian Defense chief of emergency medical service, requested the assistance of the auxiliary members in distributing equipment for the casualty centers in Norfolk. The auxiliary is sponsoring the sale of war bonds and stamps at Ames and Brownley's Department Store every Monday, and to date stamps and bonds in the amount of $27,000 have been sold. The members also serve at the sewing room of Red Cross headquarters every Friday and sponsor dances for service men at USO headquarters.

The December meeting of the Woman's Auxiliary to the Alexandria Medical Society was held at the "Laura Lee Candy House." Mrs. Stanley King, chairman of the Volunteer Special Service Committee of the Red Cross, discussed the training, duties and requirements of the "Gray Ladies." Mrs. Harrison Picot, chairman of the committee, with Mrs. C. E. Arnette and Mrs. C. V. Amole, made $25 selling pansy plants. The proceeds will go to the buying of equipment for the Alexandria Hospital. The auxiliary donated the sum of $160 to the Alexandria Laboratory for purchasing a microtone. A beautiful handmade quilt was raffled off and $25 cleared.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal. — Dr. William B. Nelson, Bay Minette, health officer of Baldwin County, has been placed in charge of the health units at both Baldwin and Escambia counties.——Austin W. Curtis Jr., for eight years assistant to the late George Washington Carver, D.Sc., director of the department of agricultural research at the Tuskegee Institute, has been named his successor.

State Committee Approves Establishment of Medical School.—The establishment of a four year medical school in Alabama was assured on January 27 at a meeting of Gov. Chauncey Sparks, Montgomery, with members of the state board of health and a special committee of the Medical Association of the State of Alabama appointed to promote the project. Tentative legislation has been drawn by the state medical association committee which would leave to a special commission to be appointed by the governor the matter of location, construction and equipment. The school will be known as the school of medicine of the University of Alabama and Dr. William D. Partlow, Tuscaloosa, chairman of the committee of the state medical association, in a statement to the press, said that it will absorb the two year premedical course now offered at the University of Alabama. Birmingham has been suggested as the location for the two years advanced training. Establishment of the school has been endorsed by the state medical association, the state board of health and every county medical society in the state. Members of the committee of the state medical association promoting the project include Dr. Partlow, chairman; Drs. Edwin V. Caldwell, Huntsville; James P. Collier, Tuscaloosa; Samuel A. Gordon, Marion; Samuel L. Ledbetter Jr., Birmingham; Burton F. Austin, Montgomery, state health officer; John H. Blue, Montgomery; Emmett B. Frazer, Mobile; Paul P. Salter, Eufaula, and Audiss M. Walker, Tuscaloosa.

CALIFORNIA

Civil Service Examination for Intern.—The Los Angeles County Civil Service Commission announces that applications for the position of intern are being accepted until April 15. There will be no written test. Candidates will be rated on their professional training and experience and their aptitude and personal suitability for internship, as evidenced by investigation or interview. All candidates must be citizens of the United States who have completed a medical course at an approved medical school in the United States or Canada within five years prior to April 15 or who will have completed the course prior to July 1, 1944. Applications may be secured from the dean of any of the accredited medical schools or full information may be obtained by writing directly to the Los Angeles County Civil Service Commission, Room 102, Hall of Records, 220 North Broadway, Los Angeles.

Memorial to Eric Liljencrantz. — The Hewlett Club of Stanford University School of Medicine, San Francisco, recently established the "Eric Liljencrantz Memorial Collection on Aviation Medicine" in the Lane Medical Library in honor of the first member of the faculty to lose his life in the present war. Dr. Liljencrantz, a commander in the medical corps of the U. S. Naval Reserve, was killed in an airplane accident while at sea near the naval air station at Pensacola, Fla., Nov. 5, 1942. He had been granted a leave of absence at Stanford, where he was assistant professor of medicine (radiology), to carry out an assignment with the Bureau of Aeronautics in the Navy Department. The *Stanford Medical Bulletin* announced that any contributions to the memorial may be sent either to Dr. Loren R. Chandler, dean of the medical school, or to Lane Medical Library.

Neurologic Bulletin Dedicated to Dr. Ingham. — The *Bulletin* of the Los Angeles Neurological Society for December was dedicated to Dr. Samuel D. Ingham, a former president of the society and clinical professor of medicine (neurology) at the University of Southern California School of Medicine, Los Angeles, as a tribute of esteem of members of the society and in recognition of his contributions to the specialty of neurology. Dr. Ingham was born in Mehoopany, Pa., in 1876. He graduated at the Medico-Chirurgical College of Philadelphia in 1899 and served on the staff there from 1907 to 1910 as instructor in neurology. He was clinical professor of nervous and mental diseases at Temple University School of Medicine, Philadelphia, from 1910 to 1920. He joined the staff of the Los Angeles County Hospital in 1921 and the faculty of the University of Southern California School of Medicine in 1931. He was chairman of the section on neurology of the California Medical Association in 1922, vice president of the American Neurological Association, 1936-1937, and chairman of the Section on Nervous and Mental Diseases of the American Medical Association, 1937-1938. He is now editor-in-chief of the *Bulletin* of the Los Angeles Neurological Society.

CONNECTICUT

Hospital News.—A temporary 50 bed wing will be erected at the Bristol Hospital, Bristol, to cost about $152,000. A grant of $67,641 was made to the hospital by the Federal Works Agency in November, according to *Modern Hospital*. The project will provide a temporary wartime addition. It will be of stone, brick, mill and frame construction. Only the walls and foundations will be permanent enough to be retained after the war.

DISTRICT OF COLUMBIA

Personal.—Rear Admiral Ross T. McIntire, Surgeon General of the United States Navy and personal physician to President Roosevelt, received the honorary degree of doctor of science at the commencement exercises at Marquette University School of Medicine, Milwaukee, February 13.

Society Adopts Civilian Medical Care Program.—A six point program to provide "adequate medical care for the civilian population in wartime Washington" was to be started immediately with a canvass of all physicians, the Washington *Star* announced on January 19. A committee on medical service for the District of Columbia was set up comprising representatives of the Medical Society of the District of Columbia, the U. S. Public Health Service, the Health Security Administration, the Emergency Medical Service for Civilian Defense and the Medico-Chirurgical Society. The plan was presented at a meeting of the district medical society on January 18 following its adoption by the newly organized committee. Its objectives are a canvass of all physicians to learn the patient load, establishment of panels of physicians for sections of the city to serve in emergencies and epidemics, and an inquiry into the system of rationing gasoline and tires (doctors say the system takes too much time from attention to the sick), educational program and preventive medicine to meet dangers of overcrowding and postwar planning. The new committee acted under the chairmanship of Dr. A. Magruder MacDonald, president of the district society and district coroner. Practical phases will be worked out geographically on the basis of the selective service map of the district, with key physicians to be assigned with responsibility for certain areas. The executive board of the district society had at this time approved the project, but it was to be submitted to the entire society for final approval at a later meeting. Meanwhile, according to the *Star*, the program was to be put into immediate action by a canvass of all physicians "to determine the patient load each medical practitioner is carrying and the demands being made on him for medical service which he is unable to meet." Specialists will be asked to do general practice in the emergency. A committee of the society had in December announced a survey of wartime medical needs of Washington (THE JOURNAL, January 9, p. 139).

IDAHO

Physicians in the Legislature.—Physicians in the present session of the Idaho legislature are Drs. Charles A. Robins, St. Maries, and John D. Shinnick, Grangeville. Dr. Robins is serving his third successive term as state senator; he was elected president pro tem.

Appointments to State Examining Board.—Gov. C. A. Bottolfsen, Boise, recently appointed the following members of the Idaho State Board of Medical Examiners: Drs. Albert B. Pappenhagen, Orofino; Frank C. Gibson, Potlatch; Casper W. Pond, Pocatello; George C. Halley, Twin Falls; Thomas A. Ellison, St. Anthony, and Samuel M. Poindexter, Boise.

IOWA

New Director of Local Health Services.—Dr. Chester L. Putnam, medical director of district health service number 8 with headquarters in Manchester, was recently appointed director of local health services for the state department of health. Dr. Donald M. Harris, Le Mars, medical director of district health service number 3, with headquarters in Spencer, was named to succeed Dr. Putnam in the eighth district.

LOUISIANA

Personal.—Dr. Herbert Randolph Unsworth was recently installed as president of the New Orleans Neuropsychiatric Club, and Dr. Guy L. Odom was chosen secretary-treasurer. ——Paul S. Lavik, Ph.D., has been appointed full time instructor in the department of biochemistry at Louisiana State University School of Medicine, New Orleans.

Dr. Matas Awarded Fraternity Medal. — Dr. Rudolph Matas, New Orleans, was recently presented with the medal of the Nu Sigma Nu degree of merit, the highest honor conferred by the fraternity. The award recognizes thirty years of service by Dr. Matas to the group as a faculty member of Beta Iota Chapter of Tulane University of Louisiana School of Medicine, New Orleans, and as president of the National Honorary Council in 1935. The only other recipients of this medal have been Drs. Frederick G. Novy, Ann Arbor; Torald H. Sollmann, Cleveland; James B. Herrick, Chicago, and the late Drs. Victor Vaughan, Detroit; Nicholas Senn, Chicago; John B. McMurrich, Ste. Anne de Bellevue, Quebec; William H. Welch, Baltimore; Gotthelf C. Huber, Ann Arbor; William H. Park, New York, and John M. T. Finney, Baltimore.

MASSACHUSETTS

Lecture on Tropical Medicine.—Col. Richard P. Strong, M. C., Army of the United States, director of Tropical Medicine, Army Medical School, Washington, D. C., delivered two lectures at the Harvard Medical School, Boston, January 26, on "Importance of Tropical Infectious Disease in the Present War" and "Diagnosis and Prevention of Plague and Cholera."

Dr. Thorn Addresses Harvey Society.—Dr. George W. Thorn, Hersey professor of the theory and practice of physic, Harvard Medical School, Boston, lectured at the Beth Israel Hospital, January 22, under the auspices of the William Harvey Society and Tufts College Medical School, Boston. His subject was "The Clinical Aspects of Sodium and Chloride Metabolism."

New Hospital House Journal.—The *News*, official house publication of the Massachusetts General Hospital, Boston, recently made its appearance. It is intended not merely as a medium of communication to the staff and personnel but to distribute information about hospital activities and to give news of individual members. The hospital distributes the *News* to all alumni now on military duty as well as to members on the active staff.

Dr. Blake Gives First Begg Society Lecture. — Dr. Francis G. Blake, dean and Sterling professor of medicine, Yale University School of Medicine, New Haven, presented the first annual Begg Society Lecture at Boston University School of Medicine, January 28, on "Epidemic Diseases in Wartime." The Begg Society was founded about a year ago by a group of third and fourth year students at Boston University School of Medicine to promote good scholarship and fellowship. The recent lecture is the first in a lectureship which the society plans to sponsor annually. The Begg Society was established in honor of the late Dr. Alexander S. Begg, who at the time of his death was dean of the school of medicine.

MINNESOTA

Interstate Shipment of Abortifacient Paste Enjoined. —On January 19 Hon. Robert C. Bell, U. S. District Judge for the District of Minnesota, signed an order granting a permanent injunction restraining the shipment in interstate commerce of a drug labeled "Intrauterine Paste" or "Dependon Products Paste" manufactured and sold by Anne M. Jenks and Jenks Physicians' Supplies, White Bear Lake. The injunction followed a trial that commenced January 5 in St. Paul. At the trial the government called forty-six witnesses, thirty-nine of whom were physicians. Of this number six were confessed criminal abortionists and a dozen or more were physicians who had used the paste in so-called therapeutic abortions. The state board of medical examiners reports that the court, in its findings of fact, found that the paste as shipped in interstate commerce was "composed mainly of potassium soap or other soft soap base, with small quantities of alcohol, iodine and distilled water added. . . ." The court also found that the paste was represented to the medical profession and others as being "safe and appropriate for introduction into the pregnant uterus, for the purpose of inducing labor, terminating pregnancy, and removing the retained portions of the products of conception." The court also found that the paste was represented as "an effective medicament for the treatment of cervicitis, endometritis, dysmenorrhea, and cervical and uterine discharges." As a result of the evidence, the court found that the paste "is unsafe and dangerous to health and has caused fatalities and serious injury. Among the specific dangers which are involved in and have resulted from its use are the extensive destruction of tissue, hemolysis or the destruction of the cellular portions of the blood, systemic potassium poisoning, extensive hemorrhage and prolonged bleeding, sterility, peritonitis, pulmonary embolism, damage to kidneys, liver and other internal organs, and increased susceptibility to infection." The court then found as a matter of law that the paste was misbranded and that its labeling was false and misleading and that "in truth and in fact it is ineffective for such purposes."

NEW JERSEY

Infectious Diarrhea of Newborn Made Reportable.—At a meeting of the state department of health, January 12, infectious diarrhea of the newborn was added to the list of reportable diseases.

Endowment Fund for Scientific Work.—Plans are under way to establish an endowment fund in the Medical Society of New Jersey "to support and encourage scientific work, as means and opportunity may be available." This activity would be carried out under the newly organized committee on scientific work of the state society which is now functioning under the chairmanship of Dr. William W. Maver of Jersey City.

Gonococcus Culture Facilities Offered to Physicians.— A new gonococcus culture service by mail was recently inaugurated by the state department of health. Culture stations have been established throughout the state where the physician, to submit a specimen to be cultured for gonococci, must first obtain a culture outfit. After the specimen is obtained from the patient the outfit must be returned to the station within three hours. At the culture station the specimen will be incubated for eighteen to twenty-four hours and mailed to the laboratory of the state department of health. According to the state medical journal, it is recommended that whenever a culture is taken a smear be taken also. It is expected that the new service will materially aid in the reduction of gonorrhea in the state. The state journal points out that chronic gonorrhea in women is often relatively asymptomatic and very frequently smears are consistently negative. Cultures will detect a much higher percentage of the cases. Cultures have an additional advantage over smears in that they differentiate the gonococcus from other gram negative diplococci which may be merely contaminants.

NEW YORK

Graduate Lectures.—Dr. Frederick N. Marty, Syracuse, will discuss "Plasma Therapy" before the Cortland County Medical Society at the Cortland County Hospital, Cortland, March 19, under the auspices of the state department of health and the state medical society. Dr. Paul Reznikoff, New York, lectured under the same auspices on March 2 at the joint meeting of the Onondaga County Medical Society and the Syracuse Academy of Medicine on "The Diagnosis and Treatment of Anemia."

New York City

Personal.—Dr. Duncan W. Clark, instructor in the department of medicine and director of the student health service, Long Island College of Medicine, Brooklyn, has been appointed assistant dean effective February 1. Dr. Clark, who graduated at Long Island College in 1936, later was a Commonwealth Fund Fellow at Yale University School of Medicine, New Haven.——Raymund L. Zwemer, Ph.D., of the Columbia University College of Physicians and Surgeons has been elected an honorary member of the Sociedad de Medicina de Montevideo, Uruguay, and a corresponding member of the Sociedad Argentina de biología of the Asociación Médica Argentina.

Dr. Calderone Named Deputy Commissioner of Health. —Dr. Frank A. Calderone, secretary of the city department of health since July 16, 1942, has been appointed deputy health commissioner to succeed George T. Palmer, Dr.P.H., who resigned on February 13. Dr. Calderone graduated at the New York University College of Medicine in 1924 and served there as instructor in pharmacology and physiology from 1932 to 1936. After receiving his master's degree in public health at Johns Hopkins University School of Hygiene and Public Health, Baltimore, in 1937 he joined the New York State Health Department as epidemiologist. Later he was district health officer at the lower east side health center and currently is lecturer in the department of preventive medicine at the New York University.

SOUTH CAROLINA

Personal. — Dr. Charles E. Ballard, Allendale, has been appointed director of the Pickens-Oconee Health Unit.——Dr. Lee W. Milford, Clemson, school physician of Clemson College, was recently elected president of the Southern Conference; he was formerly vice president of the athletic group.—— Dr. and Mrs. Joseph H. Saye observed their fiftieth wedding anniversary in Sharon, January 11.

Business Manager Appointed for State Association.— Mrs. Claude G. Watson, Florence, who for two years has been working in the secretary's office, has been elected business manager of the South Carolina Medical Association. This action was taken at a recent meeting of the council to increase the business efficiency of the association. Mrs. Watson will continue to work in the office and under the direction of the secretary-treasurer and editor, Dr. Julian P. Price, Florence.

VIRGINIA

Personal.—Dr. Robert Manton Wilson, head of the medical aid division of the Richmond Health Department, has been appointed coroner to succeed Dr. John Hamilton Scherer, who has resigned to devote his full time to private practice.—— Dr. Powell G. Dillard has been named city school physician of Lynchburg, succeeding the late Dr. John Paullett Clark.

Nutrition in Wartime.—The Medical College of Virginia announces a nutrition symposium to be held March 25-27 at the college, Richmond. Gov. Colgate W. Darden Jr. will open the program with an introduction of Dr. Irl C. Riggin, state commissioner of health, who will discuss "Nutrition Plans of the State Department of Health." Other speakers on the program will be:

Dr. William H. Sebrell Jr., Bethesda, Md., Nutrition in a Changing World.
Lydia J. Roberts, Ph.D., Chicago, Making Nutrition Vital.
Leander B. Dietrick, M.S., Blacksburg, Victory Gardens as Related to Wartime Nutrition in Virginia.
Dr. Virgil P. Sydenstricker, Augusta, Ga., Rationing as It Affects Nutrition of the Public.
Washington OPA Representative (name not announced), Living Under Rationing.

A dinner meeting will be addressed Friday evening by Dr. Sydenstricker on "Wartime Nutrition in England." The sessions will conclude Saturday morning with a panel discussion on "Teaching Nutrition Material to Elementary School Children."

WEST VIRGINIA

Dr. Crosson to Become Industrial Consultant for Sharp and Dohme.—Dr. John W. Crosson, Charleston, since 1940 director of the bureau of industrial hygiene of the state department of health, has resigned to become industrial consultant for Sharp & Dohme. He will be attached to the medical research staff at Philadelphia.

Horatio Buonanno Permanently Rejected for Licensure.—Judge Julian F. Bouchelle entered a final order, February 4, in the circuit court of Kanawha County, forever prohibiting the Public Health Council of West Virginia from further considering the application of Horatio Buonanno, Fairmont, to practice medicine and surgery in West Virginia, according to an announcement from the state medical association. The action ends the case between the state medical association versus the West Virginia Public Health Council and Horatio Buonanno, although the final order provided that nothing therein should be construed as prohibiting Buonanno from obtaining a license by means of another examination regularly held under the provisions of the code. Buonanno was licensed to practice medicine in West Virginia on Aug. 22, 1927. Prior to his admission to this examination he presented a diploma to the council which purported to show that he had successfully completed a course of study as prescribed by law, being one of the prerequisites for examination and for the issuance of a license to practice. In 1928 the council ascertained that the diploma submitted by Buonanno was from a "fraudulent" school. In 1930 the license to Buonanno was revoked on the ground that he was guilty of dishonorable conduct, having secured the license by fraud. Buonanno again appeared before the council in 1934 and presented a diploma purportedly issued by the University of Rio de Janeiro. The council learned that this diploma was not genuine and refused to reinstate the license. Since that time Buonanno has tried repeatedly to have his license reinstated. At a meeting of the council in November 1941 he was advised that the council would act on his application at the meeting to be held in March 1942. The West Virginia State Medical Association instituted a proceeding in March 1942 for the purpose of restraining the Public Health Council from further considering Buonanno's application. In a decision handed down by the Supreme Court on Dec. 8, 1942 the ruling of the circuit court of Kanawha County restraining the Public Health Council from further consideration of Buonanno's application for a license to practice medicine and surgery in West Virginia was affirmed.

WISCONSIN

Lippitt Memorial Lecture. — Dr. Marcy L. Sussman, director of the department of radiology, Mount Sinai Hospital, New York, delivered the eighth annual Lippitt Memorial Lecture under the auspices of the Mount Sinai Hospital, Milwaukee, January 22. His subject was "Newer Concepts in the Diagnosis of Congenital Heart Disease."

Orthopedic Field Clinics.—On January 1 the bureau for handicapped children of the state board of health started a series of orthopedic field clinics throughout the state for persons under 21 years of age. They will be continued until July 1, 1943. During 1941 and 1942, 1,033 children were examined at these field clinics. All referrals to the clinics for examinations must be made by the family physician. Parents and physicians are invited to attend the clinic with the child. If necessary, other services may be obtained in addition to orthopedic treatment.

GENERAL

Urologic Prize Will Not Be Awarded This Year.—The American Urological Association announces that its annual research prize of $500 will not be awarded this year and that plans for its June meeting in St. Louis have been canceled.

Meetings Postponed.—The American Association for the Study of Goiter has announced that all meetings of the association will be postponed for the duration of the war. All the present officers will hold their positions until the next meeting of the association. The 1943 session of the American College of Chest Physicians has been canceled.

Special Society Election.—Dr. Robert Chobot, New York, was recently chosen president of the Society for the Study of Asthma and Allied Conditions; Dr. Harry B. Wilmer, Philadelphia (now deceased), was elected vice president, and Dr. William Cook Spain, New York, was reelected secretary. The 1943 meeting is tentatively planned for December in New York.

Dr. McGinnes Appointed Director of Red Cross Midwestern Area.—Dr. G. Foard McGinnes, director of venereal disease control division in the Tennessee Department of Public Health, Nashville, and associate professor of preventive medicine at the University of Tennessee College of Medicine, Memphis, has been appointed director of medical and health service of the midwestern area of the American Red Cross with headquarters in St. Louis. He succeeds Dr. Howard B. Mettel, who died in November 1942. Dr. McGinnes was formerly director of the bureau of communicable disease of the Virginia State Department of Health.

New Journal on Biochemistry.—The *Archives of Biochemistry* recently made its appearance. Published by the Academic Press, New York, the new journal intends to cover the field of chemical structure and reactions of living organisms including proteins, hormones, vitamins, viruses, enzymology, biochemistry and biophysical research in chromosomes, metabolism, nutrition, photosynthesis, plant chemistry, organic chemistry as related to living organisms, colloid science in its biologic applications and chemotherapy. Manuscripts may be submitted to the editorial office of the *Archives,* 125 East Twenty-Third Street, New York, or to one of the editors:

Moses L. Crossley, Ph.D., American Cyanamid Company, Bound Brook, N. J.
Fred C. Koch, Ph.D., Armour and Company, Research Department, Chicago.
Cline M. McCay, Ph.D., Cornell University, Ithaca, N. Y.
Frederick F. Nord, D.Sc., Fordham University, New York.
Frits W. Went, Ph.D., California Institute of Technology, Pasadena, Calif.
Chester H. Werkman, Ph.D., Iowa State College, Ames, Iowa.

Foundation for the Study of Cycles Offers Prize.—The Foundation for the Study of Cycles, New York, a nonprofit organization created to foster, promote and conduct scientific research in respect to rhythmic and periodic fluctuations in any branch of science, announces the offering of a medal to the person who, during 1943, published the book or paper that in the opinion of the judges is the most outstanding. The foundation is an outgrowth of the permanent committee set up at Matamek in Canada after the first International Conference of Biological Cycles. In its present form the foundation dates from 1940, at which time it was incorporated as a nonprofit organization under the laws of Connecticut. In addition to awarding a medal, the foundation makes awards for outstanding work in each branch of science. The person who receives

the medal and the persons who receive the awards will also be elected fellows of the foundation. Additional information may be obtained from Ellsworth Huntington, Ph.D., chairman of the committee on awards, Hendrie Hall, Yale University, New Haven, Conn.

New Committee on Food Composition.—The food and nutrition board of the National Research Council has organized a committee on food composition, under the chairmanship of Conrad A. Elvehjem, Ph.D., Madison, Wis., to collect, coordinate and appraise food composition data. The committee is to act as repository and point of dissemination for authentic data on all foods being used or considered for use by all branches of the military services. Proximate and mineral composition as well as analyses for vitamins A and C, thiamine, riboflavin and niacin are required as a basis for nutritional evaluation of these foods. Data on new products, processed foods and dehydrated meats, fruits and vegetables especially are needed. The committee has already enlisted the cooperation of federal and state laboratories throughout the country. However, it is also aware that a great wealth of food composition data have been accumulated in the course of research and routine analyses by industrial laboratories. It is the purpose of this communication to appeal to these laboratories of the food industries to make their data active in the war effort. The committee assures that data received for this purpose will be handled with such reservations as should be exercised in the official utilization of this information by the armed services only. Please address Paul L. Pavcek, Ph.D., secretary, Committee on Food Composition, National Research Council, 2101 Constitution Avenue, Washington, D. C.

Special Program Marks End of Science Talent Search.—The second Science Talent Search to find potential science talent in high school graduating seniors throughout the nation ended with a special program in Washington, February 26-March 2, at which time the forty finalists, including twenty-nine boys and eleven girls, met at the Science Talent Institute to compete in final examinations for Westinghouse science scholarships. The theme of the second annual search was "Science's Next Great Step Ahead" and the recent program was designed to emphasize some things that will constitute the next great step ahead of science. One session was a panel discussion on vocational opportunities by authorities in special fields. The program included a nutrition luncheon and special broadcast over the Columbia Broadcasting System with an interview of Milburn L. Wilson, D.Sc., assistant director in charge of nutrition, Office of Defense Health and Welfare Services, by Watson Davis, director of Science Service, on "Nutrition in Wartime." At other sessions the speakers included Hugh S. Taylor, Sc.D., Princeton, N. J., on "Molecules and the Future of Chemistry"; Eleanor A. Bliss, Sc.D., Baltimore, "Advances in the Sulfonamide Drugs"; Dr. Warren H. Lewis, Philadelphia, "Cancer Cells," and Edwin G. Conklin, Sc.D., Princeton, N. J., "The Biological Future." At the banquet Dr. Thomas Parran, surgeon general of the United States Public Health Service, was among the speakers.

Research in Mental Hospitals.—The National Committee for Mental Hygiene, New York, has recently published a report on "Research in Mental Hospitals—Study Number Two," describing investigations of causes and treatment under way by five hundred investigators in seventy-nine research centers under private auspices, such as general and mental hospitals, clinics, medical schools and universities, located in thirty-nine cities and towns in twenty-two states and the District of Columbia. The first study, issued by the committee in 1938, was a survey of research in state hospitals and other tax supported institutions for the mentally ill and defective. Both surveys were made in cooperation with and through funds provided by the John and Mary R. Markle Foundation. According to an announcement these surveys are "designed to clear the way for further progress in dealing with a major medicosocial problem that takes an enormous toll both of individual lives and of individual and community wealth and that shows signs of becoming even more serious. The magnitude of the problem is reflected in a "great and ever growing demand for hospital and clinic accommodations for the care and treatment of sufferers from mental and nervous disorders." Many phases of neurotic and psychotic disorders are covered at certain research centers. Insulin and other shock therapies in treating mental disorders are studied at other centers. Some groups emphasize research on organic symptoms resulting from emotional stress and from the so-called psychosomatic disorders; others deal with industrial psychiatry, child guidance, studies of marital relations, case work with retarded and delinquent children, alcohol and drug addiction, sex variants, suicide symptoms, epilepsy, hypnosis, fever treatment in dementia paralytica, prolonged sleep therapy in psychoses and various behavior deviations as well as all types of mental disorders and treatments.

CANADA

National Program on Nutrition.—A national nutrition program was inaugurated in January, according to the *Canadian Journal of Public Health*. Educational movements were directed by the division of nutrition services of the Dominion Department of Pensions and National Health, the Wartime Information Board and the Association of Canadian Advertisers. The entire program has been designed to educate Canadians to the need of adequate nutrition for the maintenance of health and physical efficiency and arose from dietary surveys carried out throughout the Dominion.

FOREIGN

Forty Million Dollar Health Foundation.—William Richard Morris, British motor magnate and philanthropist, who bears the title of Lord Nuffield, has given $40,000,000 to form a "Nuffield Foundation." According to the Associated Press, February 13, income from this capital will be used to assist medical research and teaching, organization and development of medical and health services, scientific research, and teaching in the interests of trade and industry, pursuit of social studies, and the care and comfort of aged persons.

Deaths in Other Countries

Sir Robert Armstrong-Jones, formerly president of the Royal Medico-Psychological Association, president of the psychiatry section of the Royal Society of Medicine in 1929 and former secretary of the psychology section, Congress of Hygiene and Demography in London, died in London, January 30, aged 86. Sir Robert was first superintendent of the London County Council Asylum, Woodford, a position he held for twenty-three years. One of the Lord Chancellor's Visitors in Lunacy from 1921 to 1931, Sir Robert had been a member of the Advanced Board of Medical Studies, University of London.

CORRECTION

Annual Report of Hospital Service.—In the Philadelphia item entitled "Annual Report of Hospital Service" (THE JOURNAL, February 20, p. 610) Dr. Lucius R. Wilson should have been reported as medical superintendent of the Hospital of the Protestant Episcopal Church instead of medical superintendent of the Protestant Episcopal Church.

Government Services

Office of Indian Affairs Now in Chicago

The United States Department of the Interior announces that the Office of Indian Affairs is now located in the Merchandise Mart Building, Chicago, where it was moved from Washington. Dr. John R. McGibony, director of health, states that all communications concerning employment and health questions should be addressed to the Chicago office.

Treatment Centers for Venereal Disease

Treatment centers will be set up with Lanham Act funds in eight states, the Canal Zone and the Virgin Islands. Equipped for treating women infected with venereal disease, the centers will provide medical care designed to cure early syphilis and gonorrhea. Treatment in most cases will take about a week, with four or five weeks for observation and medical supervision. In addition to medical treatment, the centers will provide some form of vocational guidance. Attempts will be made to find profitable employment for the patients on their release and, when feasible, a certain amount of vocational training may be provided during the observation period. A center with accommodations for 200 beds is planned for the Canal Zone. Six hundred beds are planned for the three centers in Florida at Wakulla, Sarasota and Ocala; in Algiers, La., 200; Mississippi, 50; Monett, Mo., 25; Rush Springs, Okla., 50; Goldville and Pontiac, S. C., a combined 400; Knox County, Tenn., 200, and St. Thomas, V. I., 25.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Jan. 16, 1943.

Warning as to the Dose of Morphine for the Wounded

In a bulletin on the use of morphine in shock, the War Office points out that the dosage after injuries cannot be standardized, but current variations are perhaps unnecessarily wide. At times of stress the medical officer may be tempted to give considerably more than the ordinary initial dose of a quarter of a grain (0.016 Gm.) but he should remember that the ideal is to use the least dose which will be effective and that anything over half a grain (0.032 Gm.) is likely to increase the symptoms of shock and may depress the respiratory center. For severe injuries with much pain and distress an initial dose of half a grain of morphine hydrochloride or tartrate is reasonable. But, if the full dose is given, no more should be administered for at least four hours.

Disappointing results from the smaller doses are often due to poor absorption, for, in the seriously shocked, morphine may act slowly or irregularly when given subcutaneously. Intramuscular injection is preferable, and when relief of pain is urgent more use should be made of the intravenous route. An intravenous dose of ⅙ grain (0.01 Gm.) or ¼ grain (but never more), diluted to at least 1 cc. with sterile water and injected over a period of a minute or more, will reduce pain almost immediately. When injection is impossible, two ¼ grain tablets may be placed beneath the tongue.

It is also pointed out that morphine is given to many patients who would be better without it. It should be used when pain needs relief but should not be given as routine to all who seem the worse for injuries. For some of these a cup of tea would be more appropriate.

Compulsory Treatment of Venereal Disease Opposition Defeated

As usual in war there is an increase of venereal disease, which is engaging the attention of the government. Free treatment under conditions of complete secrecy has been available in Britain for twenty-five years. There are now two hundred and forty-nine treatment centers, three fourths of which are in hospitals. Eighteen new centers have been provided since the war began and five more are about to be opened. The demand for specialists and other medical staff for the fighting forces has made the staffing of the new centers difficult. There was no compulsion before the government recently made a regulation that any person who was shown to have communicated a venereal disease to two persons must attend for treatment. But this regulation has been opposed by certain politicians, mainly women. In the House of Commons Dr. Edith Summerskill (physician) moved a resolution for its annulment. She declared that it would be ineffective and would delay real action. During the last year 70,000 new cases of venereal disease came to the civilian clinics. If to these were added those which did not come, the number might be 150,000. To these must be added the number of cases in the fighting forces. The regulation would not protect the men of the country against venereal disease. No two men would inform on a respectable woman who had been infected innocently. The regulation would get only a few women, probably a few prostitutes and a few other unfortunates. She advocated the compulsory notification and treatment of all cases, as in Sweden, where the defaulter rate was only 2.5 per cent in 1935.

In the debate Sir Francis Freemantle (expert in public health) said that the question was What was going to be effective at present? The regulation was a useful step and all that could be done now. What was the good of pretending to set up clinics when we had not the doctors to man them and could not get them while the war continued? Dr. Haden Guest (physician) supported the regulation. In the fighting services, where there were both compulsory notification and compulsory treatment, there was a tremendous rise in venereal infection. Sir Ernest Graham Little (dermatologist) said that we should regard the curve of incidence of venereal disease as an epidemic. Something must be done here and now. We must get at the centers of infection here and now. The compulsory treatment of the regulation was valuable, because, although not cured of syphilis by one or two injections, a person was rapidly rendered noninfective. The resolution against compulsory treatment was rejected by a majority of 245 votes to 31.

The Phonoelectrocardioscope

A new instrument, which its inventor, G. E. Donovan, calls the phonoelectrocardioscope, was described by him in a lecture to the Institution of Electric Engineers. Though it has not yet passed out of the engineering stage, it promises to be useful to the clinician and research worker. The instrument incorporates a double beam cathode ray oscilloscope with a fluorescent screen of long afterglow, which permits the simultaneous direct visual recording of two phenomena such as the phonocardiogram and the electrocardiogram, the phonocardiogram and the sphygmogram or the electrocardiogram and the sphygmogram. At the same time the heart sounds, picked up by a special microphone, can be heard through an electrical amplifying stethoscope or a loud speaker. It is claimed that the instrument is reasonably simple to work, it cannot be damaged by overloading or shock and maintenance is simple. A further advantage is that permanent photographic records can be taken of the phonocardiogram, electrocardiogram or sphygmogram. By means of frequency filters, murmurs or other desired sounds can be accentuated and undesirable ones excluded. The instrument has an overall frequency range extending from the lowest frequency to over 1,000 cycles per second, but this band can be divided by means of filters so that the frequency response can be given any desired slope as is done in the tone control of a wireless set.

The most obvious application of the phonoelectrocardioscope is in the teaching of auscultation. Donovan states that the amplification of heart sounds through a loud speaker can never be 100 per cent satisfactory. He prefers multiple head phones, which can be used with his instrument. By means of it a group of students can hear and "see" the sounds produced by the heart, including those not audible in the ordinary stethoscope.

The Jubilee of the Clinical Journal

The centenary of the *British Medical Journal* was celebrated two years ago (THE JOURNAL, Dec. 14, 1940, p. 2099). The *Clinical Journal* has now celebrated its jubilee by a special issue which takes the place of an ordinary one and is no larger, thus keeping to the paper restrictions imposed by the war. It began publication in 1892 to provide clinical teaching by means of lectures, articles and records of cases. A series of articles by leading clinicians includes "Some Medical Aphorisms" by Sir Arthur Hurst, "Trial and Error in Endocrinology" by Sir Walter Langdon-Brown, "Irregularities of Cardiac Rhythm" by E. M. Brockbank, "Some Remarks on Perforated Peptic Ulcer" by V. Zachary Cope, "The Progress and Present Aspects of Medical Science" by Prof. J. A. Ryle, "What Do We Mean by Normal?" by Prof. D. M. Lyon, "Bleeding After the Menopause" by A. C. Palmer, "The Importance of Early Diagnosis of Cancer of the Cervix" by W. F. T. Haultain and "Practical Reflections on Some Genitourinary Conditions" by A. E. Roche. Among the congratulations, Professor Ryle refers to "this honest and helpful periodical, which goes its way unruffled by swift change or novel methods or the impatience of a specialist age."

JERUSALEM, PALESTINE

(From Our Regular Correspondent)

Jan. 3, 1943.

The Fight Against Epidemic Diseases

As a consequence of the disturbances in this country in 1936-1938 and after that of the war, a considerable increase in epidemic diseases has been recorded in Palestine. Reports published by various medical institutions convey a clear picture of the present situation. Thus in December 1942 Dr. Katzenelson gave an account of the activities of the health department of the Waad Leumi.

With regard to the present typhoid epidemic he points out that, in contradistinction to England with its population of 40 millions, less than 2,000 cases of typhoid were reported. Palestine, however, with a population of slightly more than 1½ million, had a case incidence of 2,500. In rather a small district (the Ein Geb settlement) on the trans-Jordan side of the Lake of Galilee at present 50 out of a total population of 300 are suffering from typhoid.

Braun and Dreyfuss, at the meeting of the Jewish Medical Association of Palestine, spoke about typhoid in Jerusalem in 1940-1941. Reviewing the situation from a clinical standpoint (in the "Refuah," the *Journal of the Palestine Medical Association*, May 15, 1942), they wrote as follows: A greater frequency of enteric fever was observed in Jerusalem during the second half of 1940 and during 1941. Not only in its numbers but also in its severity did typhoid and paratyphoid fever assume the character of a new epidemic. While in former years (1935-1939) no case of death occurred among 114 cases in the medical department of the Hadassah Hospital, 11 cases of enteric fever out of a total of 135 cases were fatal during the period. The clinical course was characterized by its length, its tendency to recurrences and its toxemic manifestations. Toxemia manifested itself by frequent occurrence of rigors, collapses and delirious states. The usual complications of these diseases were more frequent; besides, some rather unusual complications were observed. In a relatively large number of cases ulcerations of the throat were to be seen, in 1 case leading to extensive gangrene of the mouth and throat and so causing a lethal outcome. Other complications were hepatic jaundice, lobar pneumonia and muscular abscess. Avitaminotic states occurred quite frequently, especially of the vitamin B complex and vitamin C.

Another infectious disease which plays an important part in this country is tuberculosis. In the article referred to Katzenelson also criticizes the lack of support given by the government to the maintenance of the antituberculosis campaign. "In fighting the disease the only aid given by the government was a grant of £2,200 toward the maintenance of the Safad Hospital, whose annual budget was £10,000. Other tuberculosis hospitals received no support whatever, nor did the antituberculosis league have any help."

Nine cases of smallpox have been reported in Palestine during the last months, six of which occurred in Haifa, 2 in Beersheba and 1 in Tel Aviv. It was found that the infection had been introduced from Syria (Damas). In case of an emergency large quantities of vaccine can now immediately be made available.

Another 10 cases of plague, preponderantly in the Jaffa-Tel Aviv district, followed those reported from Haifa early in this year. Five of the patients died. Energetic measures to fight the disease were immediately taken by the government, including the establishment of a separate plague department in the Bne-Brak Hospital near Tel Aviv, to which a special plague laboratory has been attached.

Katzenellenbogen reports on vaccination against Jericho boil. Jericho boil is common among the workers of the potash plant on the Dead Sea and with the continued introduction of new labor from Leishmania-free places the problem of prophylaxis has become one of practical importance. For inoculation Leishmania tropica cultures were used which had been taken from a local case and, moreover, Leishman-Donovan bodies of the same strain from the spleens of infected Syrian hamsters.

Of 167 vaccinated persons, 152 could be kept under close observation for six to ten months. Only 7 of them developed the symptoms of leishmania, partly at the site of injection, partly elsewhere. It is assumed that in these cases vaccination coincided with the incubation period of a natural infection. The others remained healthy.

The chemotherapeutic use of halogenized phenols was studied by Bernhard Zondek at his department at the Rothschild Hadassah University Hospital in Jerusalem. In cooperation with the Teva works he was able to prepare a p-chloro-xylenol solution suited for intramuscular injection. It is a special advantage of this compound that it is bactericidal wherever it is allowed to display its activity, be it in the blood stream, where it circulates after administration, or in the urine, where it is eliminated, or even on the skin after external application. Since the active principle is absorbed by the skin, a 15 to 30 per cent ointment was prepared, 10 to 20 Gm. of which is applied on the skin on five successive days. Satisfactory clinical results with this method were recorded in pyelitis, cystitis and puerperal infection.

Palestine Health Report

Dr. H. G. H. Smart, medical adviser to the colonial secretary, who left Palestine after a short visit in September 1942, summarized some of his impressions:

"During my tour I have been much impressed by the community service that is so abundantly provided especially by the Jewish community. I have managed to learn a good deal about this and have visited Jewish hospitals and centers near Tel-Aviv at Haifa.

"I have also had the opportunity of visiting the Hadassah Medical Center recently completed after a long period of planning and careful thought. It is first class in every respect.

"The Jewish community in Palestine have a wealth of well known and highly trained scientists and doctors and they are employing this invaluable asset to the greatest advantage in the country. . . ."

Marriages

THEODORE WILLARD WEEKS JR., Moore Haven, Fla., to Miss Anna Florence Joyner of Farmville, N. C., in Baltimore, December 30.

JAMES MAC SAMS, Erwin, Tenn., to Miss Mary Elizabeth Jones of Johnson City, Tenn., in Blackstone, Va., February 5.

THOMAS STRINGFIELD JR., Waynesville, N. C., to Miss Harriet Cutler Coburn of Asheville in Biltmore, February 3.

HENRY M. WILSON JR., Peoria, Ill., to Miss Eleanor Rain of Jerseyville, Ill., in St. Louis, January 30.

EMMETT THOMAS FITZPATRICK to Miss Rose Mary Albury, both of Miami Beach, Fla., January 23.

HARRY L. ALPERT, Syracuse, N. Y., to Miss Harriet R. Ferst in Fayetteville, N. C., in January.

FRANK A. MANZIONE to Miss Mary Gabriella Kinney, both of Paterson, N. J., December 27.

WILLIAM KENNEDY KERR, Greenville, S. C., to Miss Rosa Burch in Columbia, January 26.

LESLIE E. HILDEBRAND to Miss Kathleen Corrigan, both of Spokane, Wash., December 30.

PAUL ELSBERG, Washington, D. C., to Miss Elizabeth Swartz, in Alexandria, Va., recently.

CARL B. SPUTH JR. to Miss Ruth Agnes Means, both of Indianapolis, February 10.

PAUL L. KISTNER, St. Louis, to Miss Nina Gleeson of Ferguson, Mo., February 20.

LOUIS HAMMAN to Miss Marion Campbell Bond, both of Baltimore, February 6.

Deaths

Emerson Frank Root, Salt Lake City; Western Reserve University Medical Department, Cleveland, 1880; member and past president of the Utah State Medical Association; past president of the Salt Lake County Medical Society and the Pacific Northwest Medical Society; formerly chief of staff of the Holy Cross Hospital; fellow of the American College of Surgeons; in 1930 was given a testimonial dinner by 150 members of the profession from all parts of the state to celebrate his completion of fifty years in the practice of medicine; aged 84; died, January 18, of carcinoma of the rectum and bladder.

Frederick Casimir Simon ✠ St. Louis; Missouri Medical College, St. Louis, 1899; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served during World War I and in the U. S. Public Health Service; on the staffs of the U. S. Marine Hospital, Kirkwood, the Evangelical Deaconess Home and Hospital and the Lutheran Hospital; aged 64; died, December 31, in the Veterans Administration Facility, Jefferson Barracks, of generalized arteriosclerosis and pneumonia.

Peter Whitman Rowland Jr. ✠ Memphis, Tenn.; University of Virginia Department of Medicine, Charlottesville, 1919; specialist certified by the American Board of Internal Medicine; formerly assistant professor of medicine at the University of Tennessee College of Medicine; member of the American Heart Association and the American Diabetic Association; fellow of the American College of Physicians; for seventeen years associated with the Crisler Clinic; on the staff of the Methodist Hospital; aged 49; was found dead, January 10, of acute coronary thrombosis.

Arden Cline Hornbeck ✠ Marlin, Texas; University of Texas School of Medicine, Galveston, 1920; fellow of the American College of Surgeons; past president of the Falls County Medical Society and the Twelfth District Medical Society; Federal jail physician of Falls County; local surgeon for the Southern Pacific and Missouri Pacific Railroads; examining physician for the state highway department of Falls County; chief surgeon of the Buie Clinic and the Buie-Allen Hospital; aged 45; died, January 20, of carcinoma of the spine.

William Martin Barnes ✠ Henderson, Tenn.; Memphis Hospital Medical College, 1909; aged 59; died, January 10, in the Baptist Memorial Hospital, Memphis, of pneumonia.

George Thomas Barrett, Erie, Pa.; Georgetown University School of Medicine, Washington, D. C., 1908; member of the Medical Society of the State of Pennsylvania; on the staff of St. Vincent's Hospital; aged 57; died, January 1, of cerebral hemorrhage.

Edwin Abraham Beard ✠ Inglewood, Calif.; College of Physicians and Surgeons, Keokuk, Iowa, 1898; served on the staffs of the Eye and Ear Hospital, Los Angeles, and the Centinela Hospital; aged 72; died, January 4, of coronary thrombosis.

Nahum Binderman, Brooklyn; Fordham University School of Medicine, New York, 1912; served on the staff of the Manhattan General Hospital, New York; aged 60; died, January 22, in the Israel Zion Hospital of coronary sclerosis, coronary thrombosis and pulmonary infarction.

Cluese A. Blanchard, Augusta, Ga.; University of Georgia Medical Department, Augusta, 1892; member of the Medical Association of Georgia; aged 72; died recently of coronary occlusion.

Clarence Roy Blosser ✠ Dunkirk, Ohio; Ohio State University College of Medicine, Columbus, 1912; served during World War I; aged 58; died, January 17, of cerebral hemorrhage.

Charles Jesse Brockway, Brookston, Ind.; Jefferson Medical College of Philadelphia, 1911; member of the Indiana State Medical Association; served in the medical corps of the U. S. Army in France during World War I; aged 54; on the associate staff of the Lafayette Home Hospital, where he died, January 8, of cerebral hemorrhage.

William Franklin Byler, Webb City, Mo.; University of Louisville (Ky.) Medical Department, 1904; aged 68; died, January 1, in Lebanon of hemangioendotheliosarcoma of the spleen.

James Castle, Lynn, Mass.; St. Louis College of Physicians and Surgeons, 1893; aged 85; died, January 8, of heart disease.

Louis Ballantine Chapman ✠ New Rochelle, N. Y.; Cornell University Medical College, New York, 1908; president of the medical board of the New Rochelle Hospital, where he was a member of the board of directors and associate director of medicine; at one time medical director of the Grasslands Hospital, Valhalla; aged 64; died, January 9, of coronary occlusion.

Jesse Franklin Cogan ✠ Dawson, Pa.; Baltimore Medical College, 1892; in June 1942 received a certificate for fifty years' practice of medicine from the Medical Society of the State of Pennsylvania; at one time a druggist; aged 77; died, January 1, of cerebral arteriosclerosis.

Francis James Coleman, Kuna, Idaho; Sioux City (Iowa) College of Medicine, 1897; University of Buffalo School of Medicine, 1899; aged 74; died, January 2, of arteriosclerosis.

John Philip Cooney, Providence, R. I.; College of Physicians and Surgeons, New York, 1892; member of the Rhode Island Medical Society; for many years on the staff of St. Joseph's Hospital; a member of the school committee of Providence; member of the medical staff of the St. Vincent de Paul Infant Asylum; aged 72; died, January 15, of heart disease and hypertension.

Charles P. Cooper, Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; on the courtesy staff of the Provident Hospital; aged 60; died, January 19, of cerebral hemorrhage and hemiplegia.

Robert Cowger, Danville, Ark.; Memphis (Tenn.) Hospital Medical College, 1902; aged 70; died, January 16, of heart block.

Hamilton Chalmers Cruikshank, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1919; served overseas with the Royal Canadian Army Medical Corps during World War I; deputy medical officer of health for Toronto for many years; medical officer of the Manufacturers Life Insurance Company; aged 54; died, December 25.

Charles W. Culp, Hoyt, Kan.; Beaumont Hospital Medical College, St. Louis, 1893; aged 74; died, January 12, of cirrhosis of the liver.

Arland Lewis Darling, Corning, N. Y.; University of Buffalo School of Medicine, 1892; member of the Medical Society of the State of New York; aged 72; died, December 13, of cerebral hemorrhage.

Nicholas Leeke Dashiell ✠ Baltimore; University of Maryland School of Medicine, Baltimore, 1882; aged 82; died, January 8, in the Union Memorial Hospital of injuries received when struck by a trolley car.

Charles E. Doubleday ✠ Penn Yan, N. Y.; Syracuse University College of Medicine, 1887; past president of the Yates County Medical Society; aged 78; on the staff of the Soldiers and Sailors Memorial Hospital, where he died, January 14, of cerebral hemorrhage.

Frank P. Dunn ✠ Webster Groves, Mo.; Marion-Sims College of Medicine, St. Louis, 1898; aged 72; died, January 13, of senility.

Louis Joseph Ferrara, New York; University and Bellevue Hospital Medical College, New York, 1910; member of the Medical Society of the State of New York; served on the staffs of the Fordham, Mother Cabrini Memorial and Westchester Square hospitals and University Heights Sanitarium; aged 55; died, January 19, of pulmonary fibrosis.

Merle d'Aubigne Flenner ✠ Hamilton, Ohio; Miami Medical College, Cincinnati, 1903; aged 64; member of the staff of the Mercy Hospital; served as chief of the medical staff of the Fort Hamilton Hospital, where he died, January 3, of coronary thrombosis.

Royal L. Garner ✠ Milan, Mo.; Beaumont Hospital Medical College, St. Louis, 1900; an Affiliate Fellow of the American Medical Association; aged 81; died, January 4, of arteriosclerosis and chronic myocarditis.

Thomas Cary Geron, Paris, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1901; served for many years as health officer of Lamar County; on the staff of St. Joseph's Hospital; aged 75; died, January 2, of coronary thrombosis.

Alonzo Glass, Creal Springs, Ill.; Marion-Sims College of Medicine, St. Louis, 1897; aged 83; died, January 17, of uremia and chronic nephritis.

Clark S. Glover, Russellville, Mo.; American Medical College, St. Louis, 1901; member of the Missouri State Medical Association; served as deputy state health commissioner for Cole County for many years; aged 68; died, January 5, of chronic myocarditis.

Joseph Franklin Grist, Magazine, Ark. (licensed in Arkansas in 1903); aged 73; died, December 5, of angina pectoris.

Leon Quitman Hall, Jackson, Miss.; Memphis (Tenn.) Hospital Medical College, 1913; member of the Mississippi State Medical Association; aged 55; died, December 31, in the Mississippi Hospital of angina pectoris.

Charles Benton Harpole, Evansville, Ind.; Chicago Homeopathic Medical College, 1893; at one time on the staff of the Protestant Deaconess Hospital; aged 77; died, January 10, of gastric hemorrhage.

William Gillespie Harris, Plano, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1892; member of the State Medical Association of Texas; on the staff of the McKinney (Texas) Hospital; aged 84; died, December 4, of cerebral hemorrhage.

Richard Taliaferro Henry, Springfield, Ark.; University of Arkansas School of Medicine, Little Rock, 1911; member of the Arkansas Medical Society; aged 60; died, January 4, of coronary occlusion.

Christopher Henry Herbert, Jackson, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; served on the board of trustees of the old Mississippi State Hospital for the Insane from 1900 to 1904; also a druggist; served on one of the city's first board of aldermen; aged 76; died, January 13, of arteriosclerosis.

Edward Herzog ✠ Bogota, N. J.; Univerzita Komenskeho Fakulta Lékárska Bratislava, Czechoslovakia, 1920; aged 49; died, December 27, in the Holy Name Hospital, Teaneck, of coronary occlusion.

Kenneth Jastram Holtz ✠ Seattle; Jefferson Medical College of Philadelphia, 1912; member of the Radiological Society of North America, Inc.; served as secretary of the Washington State Radiological Society; served during World War I; x-ray specialist at the Polyclinic; aged 52; died, January 9, of angina pectoris.

George Thomas Hopkins, Paragould, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; aged 73; died, January 7, of ruptured abdominal aneurysm.

William Bouldin Hopkins ✠ Jeffersonville, Ind.; University of Louisville (Ky.) Medical Department, 1921; member of the Kentucky State Medical Association; member of the staff of the Clark County Memorial Hospital; aged 51; died, January 1, in the Louisville (Ky.) General Hospital of coronary occlusion.

Simon Andrew Huber, Charter Oak, Iowa; John A. Creighton Medical College, Omaha, 1908; aged 61; died, December 10, in Sioux City of cirrhosis of the liver.

John Austin Hunter, West Middlesex, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1894; member of the Medical Society of the State of Pennsylvania; on the courtesy staff of the Christian H. Buhl Hospital, Sharon; aged 72; died, January 3, of chronic myocarditis.

J. Frank Huss, Atlanta, Ga.; Southern Medical College, Atlanta, 1894; aged 71; died, January 9, of hypertension and heart disease.

Clifford C. Johnson ✠ Harpers Ferry, W. Va.; Physio-Medical College of Indiana, Indianapolis, 1905; aged 63; died, January 18, of coronary thrombosis.

J. Leon Jones, Los Angeles; University of Wooster Medical Department, Cleveland, 1910; served in the U. S. Army during World War I; aged 58; died, January 4, of myocarditis and arteriosclerosis.

George M. Jordan, Frost, W. Va. (licensed in West Virginia in 1896); aged 87; died, December 8, of senility.

Samuel Kavinoky ✠ Buffalo; University of Buffalo School of Medicine, 1905; also a pharmacist; aged 68; died, January 23, of coronary occlusion.

Frank Emil Klauser, Toledo, Ohio; Detroit Medical College, 1879; aged 86; died, January 17, of myocardial degeneration.

Robert Keneborough Black Knowles, Vegreville, Alta., Canada; Harvard Medical School, Boston, 1902; aged 65; died, November 16.

Horace W. Kohler, Red Lion, Pa.; College of Physicians and Surgeons, Baltimore, 1911; aged 51; died, January 4, of coronary thrombosis.

Fred Herman Kruse ✠ San Francisco; University of California Medical School, San Francisco, 1915; clinical professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; member of the American Gastro-Enterological Association and the National Gastroenterological Association; fellow of the American College of Physicians; aged 63; died, January 14, of carcinoma of the prostate with metastases.

David Charlton La Grone, Midville, Ga.; University of Georgia Medical Department, Augusta, 1908; mayor of Summertown for six years; for a number of years surgeon for the Georgia and Florida Railroad; aged 57; died, January 12, in a hospital at Columbia, S. C., of cerebral hemorrhage.

Orville Nelson Lewis, Haverstraw, N. Y.; Long Island College Hospital, Brooklyn, 1903; member of the Medical Society of the State of New York; served on the staffs of the Nyack (N. Y.) Hospital and the Good Samaritan Hospital, Suffern; aged 63; died, January 9, of coronary occlusion.

Brady Forest Long, Mifflin, Pa.; Baltimore University School of Medicine, 1900; member of the Medical Society of the State of Pennsylvania; aged 69; died, November 6, in the Lewistown (Pa.) Hospital of cardiorenal vascular disease.

William Orville Manion, Portland, Ore.; College of Physicians and Surgeons, Keokuk, Iowa, 1886; served during World War I; formerly on the staff of the Veterans Administration Facility; aged 80; died, December 5, of chronic myocarditis.

Albert James Marks, Toledo, Ohio; Physio-Medical Institute, Cincinnati, 1882; Civil War veteran; aged 100; died, January 21, in the East Side Hospital of a fractured hip as the result of a fall, and senility.

Louis Lynn Marshall, Little Rock, Ark.; Eclectic Medical University, Kansas City, Mo., 1912; Kansas City (Mo.) College of Medicine and Surgery, 1916; formerly a member of the Eclectic State Medical Board; aged 61; died, January 16, of chronic lymphatic leukemia.

Robert Lee Montgomery, Tuscumbia, Ala.; Memphis (Tenn.) Hospital Medical College, 1903; member of the Medical Association of the State of Alabama; aged 72; died, December 28, of cerebral hemorrhage.

Nicholas L. Mulvey, Syracuse, N. Y.; Niagara University Medical Department, Buffalo, 1890; member of the staff of the Crouse-Irving Hospital; on the staff of the Women's and Children's Hospital, now known as the Syracuse Memorial Hospital, from 1902 to 1913; aged 81; died, January 6, of cerebral hemorrhage and colitis.

Arthur Irwin Murphy ✠ Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1908; member of the American Urological Association; aged 59; a member of the staff of the Western Pennsylvania Hospital, where he died, January 17, of pneumonia.

Paul Nathaniel Neal ✠ Raleigh, N. C.; Harvard Medical School, Boston, 1919; medical director of the Durham Life Insurance Company; aged 48; died, January 12, in the New England Baptist Hospital, Boston, of esophageal diverticulum, following an operation for mediastinal abscess, empyema and pericarditis.

Benjamin Cecil Perry ✠ Bethesda, Md.; Baltimore Medical College, 1906; member of the state board of health; at one time president of the Montgomery County Board of Commissioners; member and at one time chairman of the Maryland-National Capital Park and Planning Commission; served as vice president of the Bank of Bethesda; aged 61; died, January 8, in the Georgetown University Hospital, Washington, D. C., of chronic cardiovascular degeneration.

Alexander Fraser Pirie, Dundas, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1887; died, November 24.

John Edmond Powell, Westmount, Que., Canada; McGill University Faculty of Medicine, Montreal, 1940; commissioned a surgeon-lieutenant in the Royal Canadian Naval Volunteer Reserve; aged 25; was killed when his ship, an airplane carrier, was blown up while on convoy near Gibraltar, November 15.

Rose M. T. Reading, Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1886; aged 75; died, December 22, in Elgin, Ill., of chronic myocarditis and bronchopneumonia.

Edmonds Droke Rollins, Bristol, Va.; University College of Medicine, Richmond, 1909; aged 55; died, January 6, at his home in Bristol, Tenn., of carcinoma of the throat.

Fred Ernest Ross ✠ Erie, Pa.; University of Buffalo School of Medicine, 1897; medical director of Erie County; served on the staffs of the Hamot and St. Vincent's hospitals; aged 70; died, January 10, of heart disease.

Joseph Francis Ruiz, San Jose, Calif.; Creighton University School of Medicine, Omaha, 1939; appointed an assistant surgeon, with rank of lieutenant, junior grade, U. S. Naval Reserve, March 11, 1941; reported to a Marine division for active duty April 22, 1941; promoted to the temporary rank of lieutenant on June 15, 1942; killed in action at Guadalcanal while on duty with a Marine division, November 11, aged 27.

Pietro Sarli, Pittston, Pa.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1908; aged 63; died, November 1, in the Mercy Hospital, Wilkes-Barre, of empyema of the gallbladder and liver abscess.

Gustav Sass, New York; Medizinische Fakultät der Universität Wien, Germany, 1929; member of the Medical Society of the State of New York; aged 38; died, December 27, of sarcoma.

Joseph Scheidler, Chesaning, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1901; aged 70; died, December 3, in the University Hospital, Ann Arbor, of coronary occlusion and arteriosclerotic heart disease.

William Charles Schmidter Sr. ✠ Cincinnati; Miami Medical College, Cincinnati, 1900; aged 73; on the staffs of the Little Sisters of the Poor, Aged and Infirm, St. Francis Hospital and the Good Samaritan Hospital, where he died, December 18, following a prostatectomy.

Leo Sebastian Schumacher, Lakewood, Ohio; St. Louis University School of Medicine, 1910; on the staffs of St. John's, Evangelical Deaconess and St. Alexis hospitals, Cleveland; aged 55; died, December 13, of coronary thrombosis.

Albert Schwartz, Cincinnati; Eclectic Medical College Cincinnati, 1916; member of the Ohio State Medical Association; aged 57; died, December 19, of carcinoma of the neck.

Alexander A. Sharp, Chicago; University of Pennsylvania Department of Medicine, Philadelphia, 1886; also a lawyer; aged 80; died, December 6, in the Henrotin Hospital of coronary heart disease and general arteriosclerosis.

Charles Shattinger, Los Altos, Calif.; St. Louis Medical College, 1886; member of the California Medical Association; served on the staff of the Palo Alto (Calif.) Hospital; aged 77; died, December 13, of acute cardiac failure, chronic myocarditis and arteriosclerosis.

Hobart Parker Shattuck ✠ Los Angeles; Cornell University Medical College, New York, 1903; aged 64; died, December 10, in the California Hospital of carcinoma of the stomach.

Carl A. Sherrill, Medina, Texas; University of Tennessee Medical Department, Nashville, 1898; aged 70; died, December 15, in Galveston of coronary occlusion.

Richard Anderson Smith, Omaha; John A. Creighton Medical College, Omaha, 1915; for many years physician and surgeon for the Union Pacific Coal Company at Hanna, Wyo.; aged 53; on the staff of the Immanuel Hospital, where he died, December 18, of cerebral subdural hemorrhage, arteriosclerosis and diabetes mellitus.

August Stark, Albany, Ore.; University of Oregon Medical School, Portland, 1901; aged 78; died, December 4, in the Albany General Hospital of injuries received when struck by an automobile on November 13.

Henry Sycle Stern ✠ Richmond, Va.; Medical College of Virginia, Richmond, 1914; associate professor of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics, Inc.; member of the American Academy of Pediatrics; served with Evacuation Hospital number 18 during World War I; aged 49; died, December 24, of heart disease.

Frank Louis Stillman ✠ Columbus, Ohio; Bellevue Hospital Medical College, New York, 1881; specialist certified by the American Board of Otolaryngology; at one time on the faculty as a lecturer in the sciences at Ohio Wesleyan University; one of the founders of the Ohio Society for the Prevention of Tuberculosis; member of the American Laryngological, Rhinological and Otological Society; formerly on the staffs of the Grant and St. Francis hospitals; aged 83; died, December 23, of senility.

Thomas Thomassen Stixrud, Luebo, Belgian Congo, Africa; North Carolina Medical College, Charlotte, 1913; for many years a medical missionary with the American Southern Presbyterian Mission and was connected with the McKeown Memorial Hospital; aged 54; died, December 29, in Manchester, Mo., of coronary thrombosis.

Francis Stolle ✠ Dixon, Calif.; Stanford University School of Medicine, San Francisco, 1913; aged 55; died, December 18, of coronary heart disease.

Cornelius Francis Sullivan, Waterbury, Conn.; Georgetown University School of Medicine, Washington, D. C., 1912; served during World War I; aged 55; died, January 14, in the Veterans Administration Facility, Northport, of acute pericarditis.

Fred Charles Thum, Louisville, Ky.; Hospital College of Medicine, Louisville, 1898; Kentucky University Medical Department, Louisville, 1899; aged 68; died, December 24, in the U. S. Marine Hospital of mesenteric thrombosis and cerebral hemorrhage.

Elmer E. Thurber, Brainardsville N. Y.; University of Vermont College of Medicine, Burlington, 1886; member of the Medical Society of the State of New York; aged 81; died, December 27, in Chateaugay of arteriosclerosis.

William C. Vigor, New California, Ohio; Columbus Medical College, 1884; for many years served as clerk of the Jerome Township school board; aged 82; died, December 21, of cardiac valvular renal disease and myocarditis.

David W. Ward, Sparks, Nev.; Hahnemann Medical College and Hospital, Chicago, 1888; aged 85; died, December 26, of injuries received when he was struck by an automobile.

James Albertus Watkins, Uniontown, Ky.; Kentucky University Medical Department, Louisville, 1903; aged 68; died, January 1, of influenza and organic heart disease.

Richard Ferdinand Weirich ✠ Marcellus, Mich.; Northwestern University Medical School, Chicago, 1928; served for seventeen months in the photographic section of the air corps during World War I; member of the school board of Marcellus; served as psychiatrist at the Michigan State Hospital, Kalamazoo; member of the attending staff of Three Rivers (Mich.) Hospital; aged 47; died, December 25, in St. Luke's Hospital, Chicago, of carcinoma of the lung.

Frank A. Williams, Lake Providence, La.; Mississippi Medical College, Meridian, 1909; served during World War I; health officer of Lake Providence; aged 55; died, December 1, in Tallulah of hypertensive heart disease.

Robert Hamilton Williams ✠ Passed Assistant Surgeon, Lieutenant, U. S. Navy, Lynchburg, Va.; University of Virginia Department of Medicine, Charlottesville, 1938; was commissioned an assistant surgeon with rank of lieutenant, junior grade, U. S. Navy and later was appointed a passed assistant surgeon with rank of lieutenant; aged 32; was killed in action in the battle of the Solomon Islands, November 13.

KILLED IN ACTION

LIEUT. JOSEPH FRANCIS RUIZ, M. C., U. S. N. R., 1915-1942

LIEUT. ROBERT HAMILTON WILLIAMS, M. C., U. S. Navy, 1910-1942

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act and in cases in which they refer to drugs and devices they are designated D. D. N. J. and foods, F. N. J. The abstracts that follow are given in the briefest possible form: (1) the name of the product, (2) the name of the manufacturer, shipper or consigner, (3) the date of shipment, (4) the composition, (5) the type of nostrum, (6) the reason for the charge of misbranding and (7) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Dickson's Herb-Lax Tonic.—Addison H. Dickson, trading as A. H. Dickson, Memphis, Tenn. Shipped May 3, 1940. Composition: essentially epsom salt (approximately 28 grams per hundred cubic centimeters), small amounts of methenamine salicylic acid, sodium benzoate, plant extracts including nux vomica, and a resinous substance such as podophyllum, with a trace of iron and water flavored with peppermint oil. Misbranded because the product's name was false and misleading in representing that the mixture was a laxative compound composed entirely of herbs and derived its laxative properties solely from herbs, whereas this effect was due in part to epsom salt, a mineral substance; further misbranded because label falsely represented that the product would be helpful for indigestion, biliousness, nervousness, bad blood, rheumatism, urinary troubles and general rundown conditions.—[*D. D. N. J., F. D. C. 486; September 1942.*]

Locao Belem.—Belem Products Company, Houston, Texas. Shipped Nov. 1, 1940. Composition: chiefly water, alcohol, a foam producer, perfume materials and a small amount of glycerin. Misbranded because label falsely represented that it was efficacious in treating baldness, falling hair, dandruff and irritated scalp; that ordinary dandruff or itching scalp would respond quickly to this treatment and that satisfactory improvement or even complete elimination of these conditions would result, in from two to four weeks; that benefit would be shown in less severe cases of falling hair in a few weeks and in the more severe cases in from three to six months, and that the product would develop new growth on bald areas. Further misbranded because claim on cartons "Locao Belem has been thoroughly analyzed by the Pure Food and Drugs Department of the United States Customs and complies with rigid requirements of Pure Food and Drug Laws," was false and misleading since it had not been found by a government agency to be in strict compliance with the requirements relating to foods and drugs and it did not comply with the Federal Food, Drug and Cosmetic Act.—[*D. D. N. J., F. D. C. 487 and 507; September 1942.*]

Neff's Glan-Tex Tonic.—George G. Neff, trading as Prostex Company, Miami, Okla. Shipped between March 22 and April 1, 1940. Composition: essentially epsom salt, small amounts of ammonium alum, a mineral acid such as sulfuric acid, minute proportions of quinine, compounds of potassium and iron, and a nitrate in water. Misbranded because names "Glan-Tex Tonic" and "Prostex" in the labeling and accompanying circular were false and misleading in representing that this was a gland tonic and would be efficacious in treating prostate gland cases and kindred disorders of kidneys, bladder and urinary tract, colitis, dropsy, rheumatism and infected internal organs; that it would be of benefit in acute cases of prostatitis and dropsy and in eliminating infection and some other disorders.—[*D. D. N. J., F. D. C. 488; September 1942.*]

No-Wheez for Asthma.—No-Wheez Corporation, St. Charles, Mo. Shipped between March 1 and May 24, 1940. Composition: essentially small amounts of inorganic salts commonly found in mineral water, with pine tar and an emodin-bearing drug and water. Misbranded because label falsely represented the product's alleged efficacy in treating asthma and hay fever, in bringing lasting relief to asthma and hay fever sufferers and preventing wheezing in these conditions.—[*D. D. N. J., F. D. C. 489; September 1942.*]

Pedimoll.—Pedimoll Corporation, Los Angeles. Shipped April 25, 1940. Composition: essentially a magnesium compound with small amounts of sulfur and cresol in an oil base. Misbranded because of false and misleading label representations that it would be efficacious in treating bunions, calluses, corns, sore, swollen or sweaty feet, muscular soreness, most skin irritations, eczema and acne, athlete's foot, impetigo and sunburn; that its daily use would prevent suffering with one's feet and make walking a pleasure; that it would have a swift germicidal effect and safe, healing action; that when used on any part of the body it would relieve conditions caused by muscular soreness and strain, swelling, itching, sunburn, bruises, infected bites, sore joints, varicose veins and some other things; that by its use children would be spared suffering from corns, calluses and infections; that it would reach deeply into the pores and purge the skin of impurities; that it would be effective in the treatment of nervous, wobbly, stiff, swollen, flabby, knotty legs, would tone the circulation, soothe the nerves, loosen knotted adhesions within the muscles and foster elasticity within hardening vein walls.—[*D. D. N. J., F. D. C. 490; September 1942.*]

Correspondence

COOLING IN SHOCK

To the Editor:—Apropos of your recent editorial entitled "Cooling in Shock" (THE JOURNAL, February 6, p. 432) it may be of interest to quote from two authors of olden times. Edmund Goodwyn, M.D., writing in 1788 on The Connexion of Life with Respiration, said:

> . . . it appears on the other hand, from the result of many attempts to recover the hybernating animals from their torpor, that when the circulation of the blood has ceased, and the temperature of the body is reduced near the freezing point, if heat be applied either very suddenly, or in a very high degree, the principle of life is soon destroyed; whereas, if it be applied gradually, and in a very low degree, to the same animals in the same circumstances, the principle of life is often excited to action, and the functions are soon restored. . . .
>
> To favour the recovery then most effectually [from the state of suspended animation] the application of heat should be conducted on the same plan, which Nature has pointed out for the torpid animals. It should be applied very gradually and uniformly; and it may be raised to 98°, but not further than 100°.

John Snow, writing in 1841 on Asphyxia, and on the Resuscitation of Still-Born Children (*London M. Gaz.* **29**:222, 1841-1842) says:

> Dr. Edwards, of Paris, by a most extensive and beautiful set of experiments, . . . has found that newborn mammiferous animals die most slowly in water at about 60 degrees, which is ordinary cold water, and that they die much more quickly as the water approaches blood heat. Dr. Edwards advises that persons in the state of suspended animation should, amongst other measures, be exposed to the cool air; and that the application of heat should be avoided, unless indeed just a momentary application, to endeavour to arouse sensibility. The Royal Humane Society, however, directs the application of warmth in all practicable ways, not only as an auxiliary to artificial respiration, but even to commence with, if the means for the latter are not in readiness; and most authors, I believe, coincide with the views of the Humane Society. Dr. Edwards considers it is by its effects on the nervous system, and through that on the heart, that a high temperature produces its effects. I think that, although the nervous system may be affected, and is probably the channel of its impression, yet that the deleterious effects of an elevated temperature, when respiration is stopped, depend on its stimulating the capillary circulation of the system, and thus promoting the de-oxygenation of the blood, that change which is antagonistic of respiration, which rules its extent under all circumstances, and which, in fact, constitutes the necessity for having a respiration. But, whatever view we take of this point, the fact of the influence of temperature on asphyxia proves that the application of heat ought to be avoided until respiration is thoroughly established, when it will, no doubt, be a useful auxiliary to restore sensibility and renovate the patient.

It appears that the beneficent effect of cold in reducing the demand by the tissues for oxygen was appreciated by some thoughtful physicians over a century ago. It is possible that certain case reports in the past of recovery after long periods of extreme respiratory and circulatory depression were unjustly discredited.

RALPH M. WATERS, M.D., Madison, Wis.
Department of Anesthesia, University of Wisconsin.

PARALDEHYDE

To the Editor:—In THE JOURNAL, January 16, the page caption for Dr. Burstein's paper on Paraldehyde Administration, "Hazard of Anesthesia," is misleading. A more fitting caption would have been "Hazard of Overdosage" or "Hazard of Intravenous Dosage." Paraldehyde has been extensively used in mental hospitals as a sedative. By reputation it is the safest of hypnotics, although pulmonary complications have followed continued administration of large doses. As a preoperative hypnotic, paraldehyde is an agent of distinct value. It is suited for rectal administration in a mixture with liquid petrolatum without need for special precautions in preparing the mixture. As it is excreted almost entirely by the lungs, it has no ill effect on liver or kidneys, a point of especial importance if these organs are already diseased. In 1935, intravenous administration of pure paraldehyde as an anesthetic was suggested by Beaumachin, Springer and Elliott, but only for the briefest of operations. Their method was a proper one for the difficult subjects to be found in mental hospitals. They made trial of

doses of from 5 to 19 cc. but recommended 9 cc. as the maximum intravenous dose.

In case 1 of Dr. Burstein's paper, death occurred following intravenous administration of 35 cc. of paraldehyde. This result is not surprising, as the dose administered far exceeded the limit of safety: 35 cc. is about four times the maximum intravenous dose recommended. The margin of safety for paraldehyde administered by rectum is much greater because of the slow rate of absorption from the liquid petrolatum mixture. The preoperative rectal dosage is from 15 to 30 cc. administered with 60 cc. of liquid petrolatum an hour before the operation. This dose produces a featureless sleep for about five hours. The safety of this procedure is attested by its large margin of safety. Two patients have by mistake received 240 cc. of paraldehyde, eight times the maximum recommended dose, but have recovered without complications. Objections to the method are the penetrating odor of paraldehyde and the fact that in warm weather it attracts swarms of flies. In case 2 of Dr. Burstein's paper the fatality is attributed to rectal administration of 35 cc. of paraldehyde. While this is somewhat beyond the recommended dosage, in view of the great margin of safety of rectal paraldehyde demonstrated in other instances it is possible that the fatality was due to some factor other than the paraldehyde.

I commend Dr. Burstein for his painstaking report on paraldehyde but take this opportunity to approve somewhat an agent which, if not the safest of hypnotics, is certainly as safe as any.

ALBERT H. MILLER, M.D., Providence, R. I.

MUSCLE PHYSIOLOGY

To the Editor:—I have just read the editorial "Advances in Muscle Physiology" in the January 30 issue of THE JOURNAL. The last sentence states that the muscle of the body comprises approximately 25 per cent of the total body weight. I feel quite sure that this figure is wrong. Scammon states in the first chapter of Morris's Human Anatomy that "the voluntary musculature forms about one quarter of the body in the later part of fetal life and at birth, and increases about twofold in relative weight by maturity."

Harry A. Wilmer (Changes in Structural Components of the Human Body from Six Lunar Months to Maturity, *Proc. Soc. Exper. Biol. & Med.* **43**:545 [March] 1940) states that "the postnatal changes in the relative distribution of components consist of a marked increase in the voluntary muscle from about one fourth to over two fifths of the body mass." A graph in this article shows that muscle makes up 43 per cent of the body in the adult.

C. B. FREUDENBERGER, M.D., Salt Lake City.
Associate Dean, University of Utah School of Medicine.

OCHRONOSIS

To the Editor:—In the Dec. 19, 1942 issue of THE JOURNAL, page 1283, in an article by James W. Smith on ochronosis, the statement is made that "Harvey Cushing's finding that the first British case of ochronosis had been diagnosed Addison's disease does not appear in the medical literature and is worth recording." On page 12, volume 2 and on page 698 in the single tome edition the reference to this case is made. The case was reported by Dr. Frank M. Pope (*Lancet* **1**:24 [Jan. 6] 1906). In the front of the Jan. 6, 1906 issue of the *Lancet* are about a half dozen colored illustrations of the case. In the article itself the 11 previously reported cases are mentioned and exact references are listed. I enjoyed Dr. Smith's article but believe this is worth checking.

JAMES B. TWYMAN, M.D., Cleveland.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, Feb. 27, page 701.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 15-16. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, April 6-7. Sec., Dr. J. H. Patterson, 826 Security Building, Phoenix.

ARKANSAS: * *Medical.* Little Rock, June 3-4. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, June 3-4. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: Los Angeles, March 8-11. Sec., Dr. C. B. Pinkham, 1020 N St., Sacramento.

COLORADO: * Denver, April 7-9. *Endorsement.* Denver, April 6. Final date for filing application is March 20. Sec., Dr. J. B. Davis, 831 Republic Building, Denver.

CONNECTICUT: * Hartford, March 9-10. *Endorsement.* Hartford, March 23. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic.* Derby, March 9-10. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 13-15. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, May 10-11. Sec., Commission on Licensure, Dr. George C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, June 21-22. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, March 23-24. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, July 13. Director, Bureau of Occupational Licenses, Mrs. Lela D. Painter, 355 State Capitol Building, Boise.

ILLINOIS: Chicago, April 6-8. Superintendent of Registration, Department of Registration and Education, Mr. Philip M. Harman, Springfield.

INDIANA: Indianapolis, Sept. 14-16. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis.

KANSAS: Kansas City, May 19-20. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

LOUISIANA: New Orleans, March 11-13, May 6-8. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MAINE: Portland, March 9-10. Sec., Board of Registration in Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical.* Baltimore, March 23-26. Sec., Dr. J. T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 15-16. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, March 9-12. Sec., Board of Registration in Medicine, Dr. H. Q. Gallupe, 413-F State House, Boston.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: * Minneapolis, March 22-24. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., Minneapolis.

MISSOURI: St. Louis, March 23-25. Sec., State Board of Health, Dr. James Stewart, State Capitol Bldg., Jefferson City.

MONTANA: Helena, April 6-7. Sec., Dr. Otto G. Klein, First National Bank Bldg., Helena.

NEBRASKA: * Omaha, March 17-19. Dir., Bureau of Examining Boards, Mrs. J. Crawford, 1009 State Capitol Building, Lincoln.

NEW HAMPSHIRE: Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. Deering G. Smith, State House, Concord.

NEW JERSEY: Trenton, June 15-16. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 12-13. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NORTH CAROLINA: Raleigh, June 14-18. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, July 6-9. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, March 16-19. *Endorsement.* Columbus, April 6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, May 10. Sec., Dr. J. D. Osborn, Jr., Frederick.

RHODE ISLAND: * Providence, April 1-2. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, March 22-24. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: * Pierre, July 20. Dir., Medical Licensure, State Board of Health, Dr. J. F. D. Cook, Pierre.

TENNESSEE: Memphis & Nashville, March 24-27. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

UTAH: Salt Lake City, June. Dir., Department of Registration, Mr. G. V. Billings, 324 State Capitol Bldg., Salt Lake City.

VERMONT: Burlington, March 25-27. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, March 24-27. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WISCONSIN: * Milwaukee, March 30-April 1. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, March 16. Sec., Dr. R. L. Nugent, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, March 10-11. Sec., Dr. E. B. Starks, 1459 Ogden St., Denver.

DISTRICT OF COLUMBIA: Washington, April 19-20. Sec., Commission on Licensure, Dr. George C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, June 9. Final date for filing application is May 24. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, April 13. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MINNESOTA: Minneapolis, April 6-7. Dr. J. C. McKinley, 126 Millard Hall, Univ. of Minnesota, Minneapolis.

NEBRASKA: Omaha, May 4-5. Dir., Bureau of Examining Boards, Mrs. J. Crawford, 1009 State Capitol Building, Lincoln.

OKLAHOMA: Oklahoma City, May. Sec., Dr. Oscar C. Newman, Shattuck.

SOUTH DAKOTA: Aberdeen, June 4-5. Sec., Dr. G. M. Evans, Yankton.

WISCONSIN: Madison, April 3. Prof. Robert N. Bauer, 152 W. Wisconsin Ave., Milwaukee.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Prescribing of Drugs and Use of Surgical Instruments by Chiropractor.—Jones, a licensed chiropractor, was charged in an information filed by the prosecuting attorney of a county in Missouri of unlawfully practicing medicine and surgery in that he did attempt to treat a stated woman at a stated time and place by prescribing, dispensing and administering medicines and by using surgical instruments in performing an operation on her person. He was convicted and appealed to the Springfield (Mo.) court of appeals.

The chiropractor contended that the information on which his conviction was based was defective in that because it failed to inform him what surgical instruments were used in performing the operation alleged and what medicine or medicines were prescribed it did not enable him properly to prepare his defense. The section of the Missouri medical practice act, answered the appellate court, under which the defendant was convicted reads, so far as is here material, as follows:

> Any person practicing medicine or surgery in this state, and any person attempting to treat the sick or others afflicted with bodily or mental infirmities . . . without a license from the state board of health . . . shall be deemed guilty of a misdemeanor, . . .

The information filed in this case in charging the crime follows substantially the phraseology of the medical practice act. This is sufficient to constitute a valid charge where, as here, the statute describes the entire offense by setting out the facts constituting it. This having been done, it was unnecessary to enable the defendant properly to prepare his defense to name or describe the kind of surgical instrument or instruments used or the kind of medicine or medicines prescribed in informing the defendant of the nature of the charge against him.

The section of the medical practice act just quoted concludes with a provision that on receiving information that any of its provisions have been or are being violated the secretary of the state board of health, the agency charged with the duty of issuing and suspending or revoking licenses to practice medicine and surgery, shall investigate the matter and on probable cause appearing shall file a complaint with the prosecuting or circuit attorney in the county or city in which the alleged offense occurred. This provision, the defendant argued, sets forth the sole method by which prosecutions may be instituted, and consequently the prosecuting attorney in this case had no legal authority to file the information against him which was filed. Therefore, so his argument went, the trial court should have granted a motion he made to quash the information. The defendant's contention is untenable, said the court. True, the provision of the medical practice act just referred to does set forth a method for instituting a prosecution. This particular provision was inserted by the legislature obviously to require the state board of health to cooperate with prosecuting attorneys by giving information and filing complaints on these particular infractions of the law. This provision, however, by placing a mandatory duty on the state board of health and its secretary was designed to help prosecuting officials, not to place a limitation, restriction or check on the general powers conferred on them by law.

The chiropractor next complained of an instruction which told the jury that the practice of chiropractic is defined by the laws of the state as being the art of palpating and adjusting by hand the movable articulations of the human spinal column for correction of the cause of abnormalities and deformities of the body and that a license to practice chiropractic does not authorize the holder thereof to treat the sick by the use of operative surgery or by the administration or prescription of any drug or medicine. It was entirely proper, in view of the evidence, said the court, for the trial court to define the practice of chiropractic and to advise the jury that a license to do so would not justify the practice of medicine and surgery. There is nothing in the instruction that could have tended to prejudice the jury against the defendant.

The appellate court held further that the trial court properly refused to instruct the jury, as the defendant desired it to do, that if the jury found that the medicines furnished by the chiropractor to the complaining witness were such medicines as are generally used by the public without the prescription, "dispensation" and administration by persons licensed under the laws of the state to practice medicine and surgery, the jury should find the chiropractor not guilty. The court likewise held it proper for the trial court to permit a licensed physician and surgeon to testify that he had examined the complaining witness after she had visited the chiropractor and that he observed clots of blood and strips of tissue which indicated that the complaining witness had undergone a miscarriage or an abortion. The defendant contended that the effect of this testimony was to leave the case in such a prejudicial condition that the inference would be given the jury that the miscarriage or abortion, evidence of which was observed by this witness, had been committed by the defendant. While, said the court, it is the general rule that evidence of other crimes independent of that for which the defendant is on trial is inadmissible, where evidence of another crime tends directly to prove guilt of the crime charged such evidence is admissible. Conversely, evidence which is relevant is not rendered inadmissible because it tends to prove the defendant guilty of some other crime. As is stated in Wharton's Criminal Evidence, 11th edition, page 487, section 345:

> If the other crime and the crime charged are so linked together in point of time or circumstances that one cannot be fully shown without proving the other, regardless of whether the crime incidentally shown is of the same or a different character from the one on trial, the general rule of exclusion does not apply. . . . if evidence is competent, material and relevant to the issue on trial it is not rendered inadmissible merely because it may show that the defendant is guilty of another crime.

The judgment of conviction was accordingly affirmed.—*State v. Jones, 164 S. W. (2d) 85 (Mo., 1942).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Birmingham, April 20-22. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Association of Anatomists, Montreal, Can., April 21-23. Dr. Francis H. Swett, Box 3701, Durham, N. C., Secretary.

Arizona State Medical Association, Tucson, April 30-May 1. Dr. Frank J. Milloy, 112 North Central Avenue, Phoenix, Secretary.

Arkansas Medical Society, Little Rock, April 19-20. Dr. W. R. Brocksher, 602 Garrison Ave., Fort Smith, Secretary.

Conference of State and Provincial Health Authorities of North America, Washington, D. C., March 22-25. Dr. A. J. Chesley, 469 State Office Bldg., St. Paul, Secretary.

Florida Medical Association, Jacksonville, April 15-16. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Iowa State Medical Society, Des Moines, April 29-30. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 27-28. Dr. W. Houston Toulson, 1211 Cathedral St., Baltimore, Secretary.

Missouri State Medical Association, St. Louis, April 18-20. Mr. Raymond McIntyre, 634 North Grand Blvd., St. Louis, Executive Secretary.

Ohio State Medical Association, Columbus, March 30-31. Mr. Charles S. Nelson, 79 East State St., Columbus, Executive Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

204:625-780 (Nov.) 1942

*Syndrome Characterized by Primary Ovarian Insufficiency and Decreased Stature: Report of Eleven Cases with Digression on Hormone Control of Axillary and Pubic Hair. F. Albright, Patricia H. Smith and R. Fraser, Boston.—p. 625.

*"Epinephrine Shock" as Manifestation of Pheochromocytoma of Adrenal Medulla: Report of Case with Successful Removal of Tumor. F. L. Engel, W. H. Mencher and G. L. Engel, New York.—p. 649.

Clinical Experience with Radiophosphorus in Treatment of Certain Blood Dyscrasias. T. Fitz-Hugh Jr. and P. J. Hodes, Philadelphia.—p. 662.

Influence of Blood Transfusion and Injections of Bursa Pastoris (Shepherd's Purse) Extract on Clot Resistance in Two Hemophiliacs. A. L. Copley and J. J. Lalich, Kansas City, Kan.—p. 665.

Spinal Fluid in Tuberculous Meningitis. E. F. Traut, Chicago.—p. 670.

Gastric Lavage in Control of Treatment of Pulmonary Tuberculosis. J. J. Furlong and Mary K. Warren, Milwaukee.—p. 674.

Successful Removal of Hemangioma of Lung Followed by Disappearance of Polycythemia. J. Hepburn and J. A. Dauphinee, Toronto, Canada. —p. 681.

*Single Combined Treatment for Gonorrhea. C. Ferguson, M. Buckholtz and S. Gersten, Stapleton, N. Y.—p. 685.

*Blood Pressure and Sulfocyanates (Thiocyanate). V. S. Caviness, T. L. Umphlet and C. L. Royster, Raleigh, N. C.—p. 688.

Effect of Potassium Thiocyanate on Occurrence of Migraine. D. E. Engle and C. O. Evanson, Elmhurst, Ill.—p. 697.

Localizing Value of Clinical, Electroencephalographic and Pneumoencephalographic Findings in Epilepsy. H. Sjaardema and M. A. Glaser, Los Angeles.—p. 703.

Effect of Sulfonamides on Artificial Fever Produced by Peptone in Animals. E. M. Boyd and J. S. Pratten, Kingston, Ont., Canada. —p. 715.

Alcaligenes Fecalis Bacteremia. N. W. Voorhies and C. J. Wilen, New Orleans.—p. 719.

Effect of Hydrogen Ion and Starch Concentration of Substrate on Serum Amylase and Amylase Accelerator of Serum. W. C. Davison, Durham, N. C.—p. 723.

Significance of the So-Called P Pulmonale Pattern in Electrocardiogram. I. H. Shleser and R. Langendorf, Chicago.—p. 725.

"Essential" Hypertension: Concept of Its Mechanism. H. A. Schroeder, New York.—p. 734.

Ovarian Insufficiency and Decreased Stature.—Albright, Smith and Fraser describe a syndrome of short stature and sexual infantilism which is due to primary ovarian lack rather than to primary pituitary disease. The features which characterize this syndrome are short stature, infantile breasts, uterus and vagina, a small amount of axillary and pubic hair, good physical well being, retarded osseous development, an increase above normal of the follicle stimulating hormone and decrease of 17-ketosteroid in the urine, the development of normal amounts of axillary and pubic hair on estrogen therapy, a normal hypoglycemia responsiveness to the insulin tolerance test, frequent congenital anomalies in addition to the absence or malformation of the ovaries, diffuse osteoporosis and precocious senility. Eleven cases of the syndrome are presented. It is to be differentiated from panhypopituitarism, "premenarchal menopause precox" and a selective deficiency of the gonadotropic substance of the anterior pituitary. Evidence is presented which suggests that in females the hormone of the adrenal cortex causes axillary and pubic hair growth. Five hypotheses are discussed as causes for the syndrome. The authors believe it results from decreased functioning of the adrenal cortex caused by decreased pituitary stimulation of the adrenal cortex, which in turn results from decreased estrogen production. Turner's syndrome—congenital webbing of the neck, sexual and somatic infantilism and cubitus valgus—is a subform of this syndrome. Replacement therapy with estrogen, in addition to increasing the general well being and stimulating the growth of the breasts and axillary and pubic hair, probably leads to an increase in the rate of epiphysial growth in those subjects whose epiphyses are still ununited.

"Epinephrine Shock."—Engel and his associates describe an unusually severe instance of hyperepinephrinemia in a woman of 23, in whom attacks were induced by the most simple physiologic stimuli for epinephrine discharge such as fear, anger, before meals, during sexual intercourse and during the induction of anesthesia when aphyxia was probably the factor. The attacks, which began two and a half years ago, lasted as long as thirty-six hours, often terminating with a clinical picture suggesting so-called epinephrine shock. A pheochromocytoma was suspected. During the first exploration on the left side, anesthesia precipitated a severe attack and a phlebotomy was performed because pulmonary edema developed. Exploration failed to reveal a tumor, and the patient continued to have frequent mild attacks. Roentgen study by perirenal insufflation of 550 cc. of oxygen into the right perirenal space suggested a small mass in the right adrenal area. Preoperative preparations were made to "steal" the adrenal as is done with the thyroid in exophthalmic goiter. The renal area was exposed through a right lumbar incision and a tumor the size of a large plum was removed. As soon as the tumor was palpated, the blood pressure rose from 120 to 220 mm. systolic and remained at this level until the last vessel to the adrenal gland was ligated, when it dropped precipitously to 110 mm. and then to 70 mm. Microscopically the tumor had the characteristic structure of a pheochromocytoma. Biossay of each gram of the tumor caused a reaction in the denervated cat's iris, a retraction of the nictitating membrane and a blanching of the sympathectomized ear equivalent to that caused by 8 mg. of epinephrine. It also caused the cat's blood pressure to rise. The patient has been free from spontaneous attacks for three months. There was no evidence of insufficiency of the adrenal cortex either by electrolyte studies or from the subsequent course.

Single Combined Treatment for Gonorrhea.—To speed the recovery from uncomplicated gonorrhea Ferguson and his associates developed a high concentration of sulfathiazole in the patient and subjected him to hyperpyrexia. Their patients were seamen aged from 19 to 47 years who were infected with various gonococcus strains from many countries. The number of previous infections varied from zero to five and the duration of infection from one to sixty days. The patient, after a physical examination and the taking of cultures and smears to confirm the diagnosis, was given 1 Gm. of sulfathiazole starting at 2 p. m. and continued every four hours until a total of 5 Gm. was administered. After this he was given an enema and then a hot tub bath which brought the surface temperature to about 102 F. The patient was then put into a preheated fever cabinet and his rectal temperature was slowly raised to 106 F. This took about one hour. This temperature was maintained for about seven hours. During his stay in the hypotherm cabinet the patient was given 3 to 4 liters of isotonic solution of sodium chloride flavored with syrup. Following treatment he was warmly wrapped in blankets, brought to his room and given fruit juices and milk for the next twenty-four hours. The criteria of cure included cessation of all objective symptoms, disappearance of discharge and dysuria and a clear urine in the two glass test. For the bacteriologic and cultural examinations, on the second and then on the fourth or fifth day (for three times) after the fever therapy, a sound was inserted, the urethra was massaged gently against the sound, the sound was removed and the prostate was massaged and the strippings were examined microscopically and culturally. Three consecutive negative cultures were required for discharge. Of 25 patients with uncomplicated previously untreated gonorrheal urethritis given sulfathiazole and fever therapy 88 per cent were cured; of 20 receiving this therapy after one course of a sulfonamide compound 90 per cent were cured; of 26 receiving the combined therapy after more than one course of a sulfonamide compound 85 per cent were cured, 2 men with epididymitis recovered after one course of combined therapy and only 2 of 4 given two combined treatments recovered.

Blood Pressure and Thiocyanate.—The use of thiocyanate in the treatment of hypertension is substitution therapy. It supplies thiocyanate to hypertensive patients, who as a group have less thiocyanate in the blood than other individuals. The treatment apparently is required for life. Best results are obtained in less severe cases. Treatment should be started before there is too much sclerosis of the arterioles. Relief of symptoms can be expected in practically all cases. Functional results are good in two thirds, while one third of the patients show poor or fair results. Proper selection of patients would greatly increase the percentage of good results, but such selection is not justified because of the benefit that patients obtain from fair results and from symptomatic improvement. The underlying factor in failure is fibrosis of the arterioles and capillaries. Fair results after prolonged therapy may be had in old arteriolar sclerosis itself as well as in syphilis, hemiplegia and cardiac decompensation. Of the 136 patients of Caviness and his co-workers 92 have shown good results, i. e. a sustained reduction of at least 15 per cent in both the systolic and the diastolic pressure. Better results are obtained in private than in clinic and institutional patients. A reduction of 15 per cent is sufficient to relieve symptoms and decrease the danger of hemiplegia and angina. None of the patients have died. Best results were obtained when there was a low natural blood thiocyanate concentration, when a satisfactory response followed small doses of thiocyanate and with a blood concentration of 2.5 to 5 mg. of thiocyanate per hundred cubic centimeters of blood while on treatment.

American J. Obstetrics and Gynecology, St. Louis

44:925-1134 (Dec.) 1942

Malignancy Subsequent to Irradiation of Uterus for Benign Conditions. L. C. Scheffey, Philadelphia.—p. 925.
Functional Anatomy of Labor, with Special Reference to the Human Being. A. C. Ivy, Chicago.—p. 952.
Some Aspects of Early Human Development. J. Rock and A. T. Hertig, Boston.—p. 973.
*Effect of Progesterone in Adolescent Girls and Young Women with Functional Uterine Bleeding. W. M. Allen, St. Louis, and G. P. Heckel, Rochester, N. Y.—p. 984.
Experience of Johns Hopkins Hospital with Cesarean Section: Analysis of 1,333 Operations. C. P. Manahan, H. F. Connally Jr. and N. J. Eastman, Baltimore.—p. 999.
*Possible Etiologic Role of Gynecologic Lesions in Production of Hypertension. H. S. Everett and R. B. Scott, Baltimore.—p. 1010.
*Gonorrhea in Female and Its Treatment with Sulfonamides. R. G. Douglas, Iona F. Davis and J. F. Shandorf, New York.—p. 1026.
Studies of Human Corpus Luteum: Evidence for Early Onset of Regression of Corpus Luteum of Menstruation. J. I. Brewer, Chicago. —p. 1048.
Partial Congenital Aplasia of Vagina. W. T. Dannreuther, New York. —p. 1063.
Bacteriologic Study of Pyometra. B. Carter, Durham, N. C.—p. 1074.
Experimental Production of Toxemia of Pregnancy. F. F. Snyder, Chicago.—p. 1091.
Selective Hysterectomy for Nonmalignant Uterine Disease. E. G. Waters, Jersey City, N. J.—p. 1107.

Progesterone for Uterine Bleeding in Girls.—Menstrual records of 24 adolescent girls and young women with functional uterine bleeding to whom Allen and Heckel gave progesterone or anhydrohydroxy progesterone are listed. The effect of the drugs on the menstrual pattern was observed for many months. In general, the administration of approximately 30 mg. of progesterone (5 mg. daily) caused a cessation of bleeding within ten days of the last injection. Progesterone deprivation bleeding occurred frequently, explaining the bleeding during the first few days after therapy. In about one third of the subjects, normal cycles occurred for four months or more after therapy, whereas in another third there was a recurrence in less than four months but not in the first month. In the final third, amenorrhea followed immediately or after two or three cycles.

Gynecologic Lesions and Hypertension.—Observations which suggest that hypertension may result from partial ureteral occlusion are presented by Everett and Scott. Among the 100 women with uterine fibroids, ovarian cysts, pelvic inflammatory disease and other pelvic disorders that they studied, 36 were found to have some degree of arterial hypertension. The patients' average age was 37.06 years; only 14 of the 36 were more than 50. Further analysis revealed that 25 of those with hypertension were in the group of 50 showing pelvic and ureteral dilatation. In a study of results of appropriate treatment on the urinary tracts in 30 of these 50 patients the authors tried to find some common factor, such as infection of the urinary tract or pelvic inflammation, which might explain the failure of the urinary tracts to return to normal following treatment. Neither of these factors seemed to answer the question, and although it is difficult to show statistically it is the authors' impression that an extremely important factor was the length of time over which the gynecologic lesions in question have persisted. Therefore it seems that in the case of pelvic inflammatory disease and especially in the lesser degrees of uterine prolapse, surgical intervention should not be delayed too long. If, after a conservative regimen of palliation and chemotherapy, patients with pelvic inflammation continue to harbor masses causing the signs and symptoms of acute inflammation, the masses should be removed. A young woman with a relaxed pelvic floor and a moderate uterine prolapse should have a conservative repair operation compatible with future childbearing in preference to delaying it until her family is complete and then having a more radical procedure performed.

The Sulfonamides for Gonorrhea.—From their data on the diagnostic value of cultural and smear methods Douglas and his associates conclude that the cultural methods are superior. They compared the therapeutic value of sulfanilamide, sulfathiazole and sulfadiazine as to dosage, duration of treatment and effect of social and economic factors, pregnancy, race and age in the one hundred and eighty-five admissions of 158 patients with gonorrhea admitted to the New York Lying-in Hospital; 25 were admitted twice and 2 three times (for new infections). Sulfanilamide was used 64 times, sulfathiazole 62 and sulfadiazine 59. The latent form of the disease is often asymptomatic or associated only with leukorrhea (43 per cent) and frequently cannot be recognized without the aid of cultures. The efficacy of treatment is unaffected by age, color, pregnancy, duration of the disease or the site of the infection. Treatment and its control are more efficient if the patient is hospitalized. Of the three drugs employed, sulfanilamide was the least specific and the most toxic. Sulfadiazine appeared to be slightly more efficient and less toxic than sulfathiazole. Bacteriologic cure was most frequently encountered within nine to twelve hours after sulfathiazole or sulfadiazine and forty to fifty hours after sulfanilamide was administered. The most satisfactory therapy at present is 4 Gm. of sulfadiazine or sulfathiazole in divided daily doses for six consecutive days. Bacteriologic cure was established in one hundred and eighty of the one hundred and eighty-five admissions.

American Journal of Public Health, New York

32:1319-1434 (Dec.) 1942

Public Health and Civil Defense in Great Britain During the War. W. M. Frazer, Liverpool, England.—p. 1319.
Food and Nutrition of the Industrial Worker in Wartime. F. G. Boudreau, New York, and R. S. Goodhart, Washington, D. C.—p. 1335.
Fuel Oil Rationing Protects Public Health. J. Dean, Washington, D. C. —p. 1341.
*Etiology of Acute Illness Among Workers Using Low Grade Stained Cotton. R. Schneiter, P. A. Neal and Barbara H. Caminita, Bethesda, Md.—p. 1345.
Effect of Aluminum Hydroxide Sedimentation, Sand Filtration and Chlorination on Virus of Poliomyelitis. J. E. Kempf, Martha G. Wilson, Marjorie E. Pierce and M. H. Soule, Ann Arbor, Mich.—p. 1366.
Surveys of Nutrition of Populations: Description of Population, General Methods and Procedures and Findings in Respect to Energy Principle (Calories) in a Rural Population in Middle Tennessee. J. B. Youmans, E. W. Patton and Ruth Kern, Nashville, Tenn.—p. 1371.
Effect of Prolonged Storage on Antigenicity of Chloroform Inactivated Canine Rabies Vaccine. C. N. Leach and H. N. Johnson, Montgomery, Ala.—p. 1380.

Acute Illness Among Cotton Workers.—According to Schneiter and his collaborators, since April 1941 reports of outbreaks of an acute illness among cotton workers have been received from twenty-five states and two Canadian provinces. More than 700 cases were reported from one state alone. The illness occurred among workers exposed to high dust concentrations, and its severity varied with the degree of exposure. The illness was characterized by sudden onset, one to six hours after exposure, and the short duration of its acute phase, usually twenty-four to forty-eight hours after exposure. The principal subjective symptoms were conjunctival irritation, sub-

sternal oppression, dryness of the throat, generalized aching, fatigue, headache, cough, chills, fever, anorexia, nausea and vomiting. During the investigation one hundred and fifteen samples of cotton, cotton dust, linters, cotton plant débris, cotton seed and soil were received from fourteen states, the U. S. Department of Agriculture and two Canadian provinces. All the samples of cotton incriminated in outbreaks were dusty, low grade and stained, and they contained varying amounts of plant débris. The samples contained no toxic gases, chemically extractable substances, insecticides or pathogenic fungi, but they did contain a gram negative, rod shaped bacterium in numbers ranging from 3,000,000 to more than 10,000,000 per gram. It was not isolated from high grade cotton. Seventy of eighty-one samples of materials reported to have caused illness contained the same strain of this bacterium. The bacterium has been tentatively placed in the genus Aerobacter. A heat stable, endotoxin-like substance was demonstrated in filtrates from saline extracts of stained cotton, in filtrates from broth cultures and in killed suspensions. It is believed that this toxic substance is in the nature of an endotoxin because of its heat stability, lower antigenic capacity and increase with age of culture or destruction of cells. The severity of symptoms and physical changes was dependent on the concentration of the cotton bacterium or its products in the cotton dust inhaled and on the duration of exposure. Intradermal injections of the filtrate to man resulted in severe inflammatory lesions characteristic of acute intoxication rather than of hypersensitivity. As this acute intoxication resembles mill fever, Monday fever and gin fever in cotton mill workers, and respectively heckling fever, mill fever, grain fever and hemp fever in workers inhaling flax, jute, grain and hemp dust, the toxic products liberated by the cotton bacterium or some closely related species may be the etiologic agent for these diseases.

Arkansas Medical Society Journal, Fort Smith

39:157-174 (Dec.) 1942

"Phytobezoar": Report of Case. A. F. Hoge, Fort Smith.—p. 157.

39:175-192 (Jan.) 1943

The Kidney in Hypertension. W. J. McMartin, Omaha.—p. 175.

Bulletin of Johns Hopkins Hospital, Baltimore

71:315-388 (Dec.) 1942

Topical Projection of Nerve Fibers from Local Regions of Cochlea to Cerebral Cortex of Cat. C. N. Woolsey and E. M. Walzl, Baltimore.—p. 315.

Effect of Low Oxygen Tension on Development of Experimental Tuberculosis. A. R. Rich and R. H. Follis Jr., Baltimore.—p. 345.

Serum Proteins in Sarcoid: Electrophoretic Studies. A. M. Fisher and B. D. Davis, Baltimore.—p. 364.

Additional Evidence of Role of Hypersensitivity in Etiology of Periarteritis Nodosa: Another Case Associated with Sulfonamide Reaction. A. R. Rich, Baltimore.—p. 375.

California and Western Medicine, San Francisco

57:341-392 (Dec.) 1942

Abortion: Inevitable and Incomplete: Study of 500 Cases. J. W. Ravenscroft, San Diego.—p. 346.

Foreign Body Localization by X-Rays. E. R. Miller, San Francisco.—p. 349.

Carcinoma of Fallopian Tube. T. S. Kimball, H. E. Sanford and A. F. Brown, Glendale.—p. 351.

Contact Stomatitis Due to Denture in Metal Sensitive Patient. K. J. Deissler and G. R. Sheets, Oakland.—p. 354.

Toxemias of Late Pregnancy: Outlines of Therapy. E. W. Page, Berkeley.—p. 355.

Canadian Public Health Journal, Toronto

33:565-606 (Dec.) 1942

Food Makes a Difference. L. B. Pett, Ottawa, Ont.—p. 565.

Nutrition in War Industry. Florence Ignatieff, Toronto.—p. 571.

Immunization Program in the Royal Canadian Air Force. A. H. Sellers.—p. 575.

Individual Variation in Immunity: Variance of Antitoxic Response in Guinea Pigs Inoculated with Diphtheria Toxoid. Dorothy J. Stewart and F. G. Jones, Indianapolis.—p. 588.

Incidence of Trichomonas Vaginalis in Clinic Patients at the Women's College Hospital, Toronto. E. Kuitunen-Ekbaum and Eva Mader Macdonald, Toronto.—p. 593.

Iowa State Medical Society Journal, Des Moines

33: 1-40 (Jan.) 1943

Carcinoma of Stomach: Early Recognition and Results. J. T. Priestley, Rochester, Minn.—p. 1.

Primary Fractures of Hip. H. F. Dolan, Anamosa.—p. 5.

Recurrence of Scurvy. R. H. McBride, Sioux City.—p. 7.

Minimal Criteria of Coronary Disease. C. E. Harris, Grinnell.—p. 10.

Genital Prolapse. R. M. Collins, Council Bluffs.—p. 11.

Inguinal Hernia. B. J. Moon, Cedar Rapids.—p. 13.

Journal-Lancet, Minneapolis

62:419-466 (Dec.) 1942

Important Advances in Physiology of Sex Hormones. L. T. Samuels, Minneapolis.—p. 419.

Methods of Measurement of Naturally Occurring Sex Hormones. Clara M. Szego, Minneapolis.—p. 423.

Endocrine Factors in Menstruation and Its Relation to Dysmenorrhea. Nora Winther, Minneapolis.—p. 428.

Irregular Shedding of Endometrium. J. L. McKelvey, Minneapolis.—p. 434.

Relation of Sex Hormones to Climacterium. Della G. Drips, Rochester, Minn.—p. 437.

Relation of Hormones to Lactation. W. E. Petersen, St. Paul.—p. 442.

Intersexual Manifestations of Nonendocrine Origin. M. H. Hoffman, St. Paul.—p. 446.

Evaluation of Clinical Use of Male Sex Hormone. C. E. Rea, St. Paul.—p. 449.

*Hormones and Carcinoma of Prostate. C. D. Creevy, Minneapolis.—p. 452.

"Prefabricated Eschar" or Bandage, Containing Sulfonamide, for Treatment of Burns. W. G. Clark, E. A. Strakosch, Minneapolis, and L. N. Leven, St. Paul.—p. 455.

Hormones and Carcinoma of Prostate.—His own experience with estrogen in about 60 patients with prostatic carcinoma is still too meager for Creevy to draw definite conclusions, but he is convinced that the work of Huggins and his followers constitutes a major contribution to the comfort of old men and that its full possibilities are to be explored. Some investigators have reported the disappearance of all the characteristics of prostatic cancer on rectal examination and of metastasis to bone on roentgen examination, but he has seen both regress but not disappear. Estrogens should be tried in every case of prostatic cancer not in the gland itself, and if they fail only then should castration be performed.

Journal National Malaria Society, Tallahassee, Fla.

1:1-182, 1942

Species Eradication: Practical Goal of Species Reduction in Control of Mosquito Borne Disease. F. L. Soper; and D. B. Wilson, Toronto, Canada.—p. 5.

Anophelines of Southwestern Yunnan and Their Relation to Malaria. W. C. Sweet, L. C. Feng, C. Y. Chow and S. C. Hsu.—p. 25.

Observations on Malaria Around Lake Wilson, 1934-1941. R. B. Watson, Helen C. Maher and Margaret E. Rice, Wilson Dam, Ala.—p. 33.

Crushing Strength of Biologic Films on Natural Waters and Spread of Larvicidal Oils. C. E. Renn.—p. 45.

Malaria Control, Ditch Lining Experience in a South Georgia County. J. Andrews, R. S. Howard Jr. and E. A. Turner, Atlanta, Ga.—p. 57.

Circular Joint and Concrete Form Design for Precast Inverts for Malaria Control Ditch Lining. W. A. Legwen and Louva G. Lenert, Atlanta, Ga.—p. 69.

Design and Application of New Type Automatic Siphon for Malaria Control. W. A. Legwen and R. S. Howard Jr., Atlanta, Ga.—p. 83.

Studies on Artificial Resting Places of Anopheles Quadrimaculatus Say. M. H. Goodwin Jr., Newton, Ga.—p. 93.

Studies on Choice of Medium for Oviposition by Anopheles Quadrimaculatus Say. H. O. Lund, Newton, Ga.—p. 101.

Review of Recent Publications on Prophylaxis and Treatment of Malaria. H. C. Clark, Panama, Republic of Panama.—p. 113.

*Malaria Mortality in Southern United States for Year 1940, with Supplementary Data on Malaria in Other States. E. C. Faust and Lois De Bakey, New Orleans.—p. 125.

Human Malaria. H. W. Brown, Chapel Hill, N. C.—p. 133.

Review of Recent Work on Parasitology of Simian Malaria Infections and Simian Plasmodia. J. C. Swartzwelder, New Orleans.—p. 141.

Review of Recent Work in Avian Malaria. M. D. Young, Columbia, S. C.—p. 149.

Entomologic Work During 1941 Bearing on Malaria Problem. S. J. Carpenter, Camp J. T. Robinson, Ark.; T. T. Brackin Jr., Jackson, Miss., and D. F. Ashton, Raleigh, N. C.—p. 157.

Report of Subcommittee on Engineering. D. B. Lee, J. C. Clark, J. H. O'Neill, S. L. Davies and C. N. White, Jacksonville, Fla.—p. 163.

Malaria Mortality in the Southern United States.—Faust and De Bakey believe that the low malaria mortality rate for 1940 helps in discovering the chronic foci of the disease. Analysis of the malaria mortality data for the United States, especially for the Southern states, reveals a continued reduction, especially since 1938, to an apparently all time

average low of 3.02 for the fourteen endemic malaria states in the South. With a population of one third of the entire nation, the South had 96 per cent of the reported malaria deaths in 1940. These deaths occurred in 34 per cent of the counties in the fourteen states. There has been a favorable reduction in the number of counties in the South contributing to deaths. There was an apparent suppression of the five to seven year cyclic increase, which should have occurred in 1938-1940 in the South, in malaria deaths. The factors responsible for the decrease in rate since 1938 are unknown but may be due to better economic conditions of the poor, that is, better food, more funds for the purchase of antimalarial drugs and the screening of homes. Also intensive measures have been carried out to suppress or to reduce the number of Anopheles mosquitoes. Evidence indicates that vivax malaria has similarly decreased. The present reduced trend should not tend toward complacency, as reduced control may allow recrudescences to occur in endemic foci. As long as susceptible malaria mosquitoes breed, new infections may be introduced from tropical America and thus "seed" the country with new, possibly more virulent strains of malaria plasmodia. Possibly with continued treatment of malaria patients in endemic foci the gametocyte rate may become so low that mosquito infection will be difficult, leading temporarily to a condition of anophelism without malaria. Outside the Southern states there were only fifty-seven malaria deaths in the United States in 1940. Several of these were of drug addicts, while many of the others were probably the result of exposure to infection in the South or in tropical America.

Journal of Nutrition, Philadelphia

24:503-614 (Dec.) 1942. **Partial Index**

Periodic Administration of Anterior Pituitary Extract as Affecting Metabolism of Rats on Diets of Different Composition. Helen E. Archer, M. Kriss and L. Voris, State College, Pa.—p. 535.

Metabolism of Arginine and Leucine, with Special Reference to Respiratory Exchange and Heat Production. M. Kriss and R. S. Bowman, State College, Pa.—p. 547.

*Evaluation of Nutritional Status of Population Group in Madrid, Spain, During Summer of 1941. W. D. Robinson, J. H. Janney, New York, and F. Grande (Covian), Madrid, Spain.—p. 557.

*Effects of Diet Deficient in Part of Vitamin B Complex on Men Doing Manual Labor. R. E. Johnson, R. C. Darling, W. H. Forbes, L. Brouha, E. Egaña and A. Graybiel, Boston.—p. 585.

Relationship Between Vitamin A and Iodine Metabolism in Rat. R. E. Remington, P. L. Harris and C. L. Smith, Charleston, S. C.—p. 597.

Nutritional Status Evaluation in Madrid.—A study of the nutritional status of 561 persons of a low economic level was carried out by Robinson and his colleagues in an industrial suburb of Madrid during the summer of 1941. The combined dietary records of the family food consumption indicated an average intake of calories and calcium far below maintenance levels, and a protein intake of questionable adequacy. The levels of iron, phosphorus, thiamine and ascorbic acid appeared generally adequate for maintenance; those for vitamin A and riboflavin were at or below the borderline. Clinical examination revealed almost universal evidence of quantitative (caloric) underfeeding. Classic deficiency disease was rare: there were 2 instances of nutritional edema, 1 of chronic pellagra and 3 of rickets. Search for the early manifestation of these diseases disclosed a significant number of persons with cutaneous lesions attributable to vitamin A deficiency and a fairly high incidence, especially among the females, of capillary invasion of the cornea which was probably due to ariboflavinosis. In addition, many of the persons had signs and symptoms of a mild neural or neuromuscular disturbance of undetermined origin. About one third of the subjects had a mild macrocytic hyperchromic anemia, and the incidence of hypoproteinemia among males was 11 and among females 5 per cent.

Vitamin B Complex and Manual Labor.—Johnson and his co-workers subjected 10 men to hard daily physical work on a diet deficient in parts of the B complex, notably thiamine. During the first week of the experiment 5 of the men were given daily 2 mg. of thiamine hydrochloride; the other 5 were given placebos. During the third week (one week was spent in preliminary observations with the men on a normal diet) of the experiment all subjects received daily doses of 18 Gm. of brewers' yeast containing 0.5 mg. of thiamine. At the end of the second week all subjects complained of easy fatigue and their physical fitness had definitely deteriorated; this was greater in the subjects not given thiamine hydrochloride, most of whom exhibited symptoms, sometimes acute, of muscular and articular pains, lack of well being, poor appetite and constipation. These symptoms were mild or absent in those receiving thiamine. All these symptoms disappeared during the week that brewers' yeast was taken. The usual level of fitness was regained more rapidly and more completely by the subjects who had received thiamine during the first week. Changes in the electrocardiograms of certain subjects in both groups, noticed at the end of the deficient period, disappeared by the end of the yeast period. At the end of the week the daily urinary excretion of thiamine by those who had not received this vitamin was well within the range of deficiency. The conclusions are that when men are doing hard physical work, even for a few days, it is imperative that they have an adequate daily intake of the whole vitamin B complex if physical fitness is to be maintained. Of the vitamin B complex, thiamine alone will not maintain physical fitness of laborers in single daily doses of 2 mg., but brewers' yeast appears to be a complete and adequate supplement for a diet grossly deficient in the vitamin B complex. When the addition of vitamin B complex to a ration (as in emergency rations of troops and sailors separated from bases) is indicated, yeast would seem to be a certain source of all the necessary components.

Journal of Thoracic Surgery, St. Louis

12:109-208 (Dec.) 1942

Hemoptysis in Metastatic Tumors of Lung Simulating Bronchiogenic Carcinoma: Report of Two Cases. S. O. Freedlander and J. Greenfield, Cleveland.—p. 109.

Thoracic Gastric Cysts: Report of Two Cases with Review of Literature. H. Schwarz 2d and C. S. Williams, St. Louis.—p. 117.

Tuberculoma of Mediastinum: Report of Case. A. J. Grace, London, Ont., Canada.—p. 131.

Cancer of Trachea: Fifteen Years After Treatment for Cancer of Larynx. W. L. Watson, New York.—p. 142.

*Decompression of Chest for Dysphagia Due to Marked Cardiac Enlargement. F. C. Newton and S. A. Levine, Boston.—p. 151.

New Instruments: Description of Two Gadgets of Value in Thoracic Surgery. R. Adams and E. D. Churchill, Boston.—p. 158.

Postpneumonic Empyema in Infants and Children. M. H. Williams, Binghamton, N. Y.—p. 160.

Method of Preventing Perforation in Esophagoscopy: Treatment by Open Drainage: Thirty-Nine Cases, One Death. M. S. Lloyd, New York.—p. 186.

Spinal Anesthesia in Thoracoplasty. V. D. Schaffner and E. M. Found, Kentville, N. S., Canada.—p. 190.

Blood Loss in Thoracic Operations. M. L. White Jr. and R. W. Buxton, Ann Arbor, Mich.—p. 198.

Decompression of Chest in Dysphagia.—Newton and Levine report a case in which pronounced dilatation of the heart, especially of the left auricle, due to rheumatic valvular disease caused dysphagia. The chest was decompressed by removal of portions of the third, fourth and fifth ribs anteriorly. The dysphagia disappeared and there was a distinct improvement in the condition of the heart: palpitation was less troublesome, the heart rate could be slowed more satisfactorily and the patient's general strength improved. The patient lived for almost nine years after the operation. At necropsy the heart was found to be substantially dilated; it weighed 590 Gm. There was decided mitral insufficiency with slight stenosis, and slight stenosis of the aortic and tricuspid valves. The pericardial cavity was entirely obliterated by thin, old fibrous adhesions. The esophagus was displaced slightly to the right.

Laryngoscope, St. Louis

52:923-1000 (Dec.) 1942

Neurologic Complications of Serum Sickness, with Special Reference to the Ear. H. M. Taylor, Jacksonville, Fla.—p. 923.

Practical Aids in Technic of Catheterizing, Lavaging and Injecting Sphenoid Sinus. J. C. Peele and F. E. LeJeune, New Orleans.—p. 933.

Cricopharyngeal Spasm. L. H. Clerf and F. J. Putney, Philadelphia.—p. 944.

Pathologic Changes of Temporal Bone in Osteomyelitis of Skull. H. Brunner, Chicago.—p. 954.

Cancer of Esophagus: Study of 100 Consecutive Cases. P. H. Holinger, Chicago, and H. J. Hara, Hinsdale, Ill.—p. 968.

Presentation of Simple Device for Excluding Interfering Noises from One Ear While Testing Hearing Acuity of Other Ear. H. Newhart Minneapolis.—p. 983.

Hematology. J. J. Shea, Memphis, Tenn.—p. 984.

Suffocation by a Sunflower Seed. G. B. Gilmore and M. D. Grant, New York.—p. 993.

Medical Annals of District of Columbia, Washington

11:465-504 (Dec.) 1942

Health of Civilian Population During War: The National Problem. J. W. Mountin, Bethesda, Md.—p. 465.
Public Health Control of Venereal Diseases in District of Columbia. R. A. Vonderlehr, Bethesda, Md.—p. 471.
War Injuries of Head. W. M. Craig, Rochester, Minn.—p. 474.
Importance of Laboratory Examinations in Administration of Sulfonamides. T. M. Peery, Washington.—p. 479.

New England Journal of Medicine, Boston

227:893-938 (Dec. 10) 1942

*Skin Disturbances in Diabetes Mellitus: Their Relation to Vitamin Deficiencies. A. Rudy and R. Hoffmann, Boston.—p. 893.
Mesenteric Thrombosis in Mentally Ill Patients. C. Bell, W. Corwin, O. J. Marcil and E. V. Semrad, Waltham, Mass.—p. 901.
Male Sterility. W. W. Williams, Springfield, Mass.—p. 905.
Wound Healing. A. D. Holmes, Boston.—p. 909.

Cutaneous Disturbances in Diabetes Mellitus.—Rudy and Hoffmann present 5 case reports which demonstrate that the cutaneous disturbances in diabetes mellitus are most frequently due to a vitamin deficiency, especially that of nicotinic acid. The authors have seen many more diabetic patients with similar more or less pronounced cutaneous eruptions. The skin of some of these diabetic patients is not unlike that of pellagrins. Its vulnerability to any kind of external irritation (rubbing or other mechanical or chemical trauma, perspiration, heat or sunlight) and to infections, especially those due to monilia, is increased. Vulvitis as well as pruritus vulvae and ani in diabetes are proved signs of pellagra and are due to a nicotinic acid deficiency. The most frequent manifestation is a vivid, more or less indurated, erythema characterized by a violaceous or brownish color and a definite shiny surface. Fine lamellar peeling or psoriasiform scaliness, more or less deep ridging of the papillary lines and fissuring, edema, blistering, maceration and even superficial ulceration vary the morphologic picture. Superinfection with monilia on predisposed regions suggests intertrigo or paronychia. Pruritus vulvae in diabetes does not respond to local treatment and does not always clear up with the control of glycosuria. In the authors' patients improvement followed the administration of nicotinic acid or its amide with, and at times without, the addition of vitamin B complex. This occurred even in the presence of glycosuria and hyperglycemia. Nicotinic acid, like thiamine chloride, is essential for the satisfactory oxidation of carbohydrate foods. This explains why some cutaneous manifestations appear for the first time or become aggravated after the diabetes is controlled. In such cases the symptoms disappear with the addition of the nicotinic acid. The same happens with other vitamins, such as riboflavin and thiamine hydrochloride. It is not unusual for a neuritis or perlèche to become manifest or aggravated following the control of the diabetes or diabetic acidosis. The vitamin deficiency in diabetes mellitus may affect the gastrointestinal tract including the mouth, the central and peripheral nervous system and the genitourinary tract. The degree of the cutaneous infection depends on the severity of the vitamin deficiency and not on the glycosuria or hyperglycemia. The predisposing factors in the development of deficiency in diabetes mellitus are a diet deficient in the components of the vitamin B complex, disturbance of absorption and assimilation, and impaired hepatic function. The precipitating factors may be loss of weight, infection, gastrointestinal disturbance, operations, acidosis and intemperance.

227:939-974 (Dec. 17) 1942

Bacteriology of Wounds of Compound Fractures of Skull. D. Munro, Boston.—p. 939.
*Plasma Prothrombin and Liver Function During Sulfonamide Therapy. I. Kapnick, J. D. Stewart and C. Lyons, Boston.—p. 944.
Simultaneous Hyperfunction of Thyroid and Parathyroid Glands. E. S. Miller and L. R. Evans, Boston.—p. 949.
Complete Situs Inversus: Report of Case with Calcareous Aortic Stenosis and Cor Bovinum. J. G. Pasternack, Staten Island, N. Y.—p. 953.
Pathology: Diseases of Bone. T. B. Mallory, Boston.—p. 955.

Plasma Prothrombin and Hepatic Function.—The hepatic function, as measured by the prothrombin, van den Bergh and bromsulphalein tests, was determined by Kapnick and his associates for 68 patients receiving sulfonamide therapy for acute infection. There was a significant decrease in the prothrombin level of 14 patients during chemotherapy. The severity of the infection seemed to be more significant as the cause of prothrombin depression than did the type of sulfonamide used. A decreased prothrombin time may be the consequence of factors other than impaired hepatic function. Since serious infection and the sulfonamides are prejudicial to the welfare of the liver, it seems that some test of hepatic function should be used as a routine procedure with this group of patients. A decrease in plasma prothrombin is found early in impending hepatic failure. It is suggested that prothrombin determinations by the Quick method be done every three days on seriously ill patients receiving sulfonamide therapy. In this way patients in whom serious hepatitis is apt to develop would be recognized before the symptoms became clinically alarming.

New York State Journal of Medicine, New York

43:1-96 (Jan. 1) 1943

Epicondylitis Humeri. K. G. Hanson, New York.—p. 29.
Spinal Fluid Examinations: Report of Investigation of Procedures Followed Throughout the United States. W. B. Long and J. A. Goldberg, New York.—p. 34.
Surgery in the Aged. F. W. Bancroft, New York.—p. 37.
Outbreak of Acute Fluoride Poisoning. H. S. Ingraham, Kingston, and A. J. Flood, Coxsackie.—p. 41.
Studies in Thromboembolization: II. Observations on Use of Dicumarol [3,3'-Methylene-Bis-(4 Hydroxycoumarin)] in Embolization: Report of Five Cases. S. Shapiro and B. Sherwin, New York.—p. 45.
Role of Liver in Surgery. A. O. Whipple, New York.—p. 53.

North Carolina Medical Journal, Winston-Salem

3:623-670 (Dec.) 1942

*Pleural Reflex Syncope and Air Embolism in Artificial Pneumothorax. Allison L. Ormond, Black Mountain.—p. 623.
*Early Diagnosis of Shock. C. L. Royster, Raleigh.—p. 628.
Treatment of Chronic Alcoholism. M. A. Griffin, Asheville.—p. 632.
Intramural Postgraduate Education in Obstetrics for Practicing Physicians. A. W. Makepeace, Chapel Hill.—p. 633.
Treatment of Congestive Heart Failure. C. H. Armentrout, Asheville.—p. 636.
Advances and Limitations in Treatment of Gonorrhea in the Female. J. B. Lounsbury, Wilmington.—p. 640.
New Physical Sign in Infarction of Lung. R. L. McMillan, Winston-Salem.—p. 642.
Pentosuria. D. N. Stewart, Hickory.—p. 643.
The Hot Douche. C. A. Anderson, Burlington.—p. 644.

Pleural Reflex Syncope and Air Embolism in Pneumothorax.—Although concrete evidence proving the existence of pleural shock is not to be found in the literature, Ormond believes that the condition exists. He reports 5 cases of this symptom complex; 2 were possibly due to pleural shock and in 3 there was definite air embolism. The symptoms of pleural shock are generally indistinguishable from those caused by air embolism. The symptoms usually appear suddenly at a moment when the needle is entering or leaving the pleural space. The psychic symptoms are giddiness and loss of consciousness; the motor, tonic and occasionally clonic spasms, flaccid paralysis with contractions, hemiplegia or monoplegia, and the circulatory and respiratory symptoms are rapid, weak, irregular pulse, pallor of the skin and cyanotic patches over the face, neck and thorax. Pleural shock should be spoken of only when embolism can be excluded. One example of the existence of pleural shock is the patient with tuberculous empyema, whose chest has to be repeatedly aspirated and who goes into mild shock when the visceral pleura is irritated. Pleural shock has been observed in oleothorax, pleural exploration, pleural tap and simple pleural lavage. Many of these accidents in the pneumothorax procedures may be avoided by the proper choice of patients, proper examination, careful study of the roentgenograms, use of proper instruments and careful manometric readings.

Early Diagnosis of Shock.—It is more important to detect the earliest signs of shock, says Royster, than to know the advantages and disadvantages of the various available means for combating it. A cold and clammy skin, rapid and thready pulse, low or absent blood pressure and ashen pallor are not signs of shock but of impending death. These signs indicate that the condition is approaching or has reached the point of becoming irreversible. The common denominator of all theories of the production of shock and all systems of treatment is a decrease in blood volume in relation to the total capacity of the circulatory bed. Whatever the remote factors involved, the

peripheral circulatory deficiency which manifests itself as shock results from a disparity between the circulating blood volume and the volume capacity of the vascular system. Continued operation of the factors causing fluid loss depletes the stores of sodium in the interstitial spaces, and the delicate balance between the predominance of sodium outside the body cells and the predominant potassium within them is upset. In developing shock the two ions may effect a startling reversal. In simple, uncomplicated and not profuse hemorrhage the patient responds well to the introduction of whole blood, saline solution or plasma. The normal or artificial compensation results in hemodilution. Hemoconcentration is the earliest practicably measured change which occurs in shock. If unchecked, further hemoconcentration results and the vascular system becomes more constricted. The process is still reversible, provided the causative factor is not too overwhelming or too persistent in its action. The intravenous introduction of plasma or whole blood will usually save the patient, even though these elements are often lost through the damaged capillary walls. With excessive amounts of fluid loss and vascular damage a point is reached at which further vascular constriction is no longer possible. The reduced circulatory pressure results in tissue anoxia, and tissue anoxia causes a further demand on the capillaries for dilatation and permeability. To wait for a fall in blood pressure before diagnosing and treating shock is like waiting for general peritonitis to develop before making the diagnosis of appendicitis. Hemoconcentration appears sooner than any measurable fall in blood pressure. It takes no more time than it does to make a leukocyte count. Another method of arriving at the same conclusion is by determining the hematocrit. This reading roughly parallels the erythrocyte count in nonanemic persons. The use of the densimeter to determine the falling drop time takes only two or three minutes. The advantage of this apparatus is that in one operation the density of the blood is determined and a quantitative estimate of the type of fluid necessary is obtained. The hemoconcentration test can be used for following the effect of treatment.

Pennsylvania Medical Journal, Harrisburg

46:177-304 (Dec.) 1942

Medical Profession's Part in the War Industrial Effort. O. J. Johnson, Chicago.—p. 191.
Wartime Medicine and Selective Service. L. G. Rowntree, Washington, D. C.—p. 194.
Interpretation of Draft Rejection Figures. W. W. Bauer, Chicago.—p. 204.
Diagnosis and Surgical Aspects of Carcinoma of Colon. T. E. Jones, Cleveland.—p. 208.
Clinical Use of Tuberculin. W. E. Nelson, Philadelphia.—p. 213.
Infectious Eczematoid Dermatitis. D. L. Cooper, Erie.—p. 218.
Surgical Management of Spinal Cord Trauma and the Neurogenic Bladder. T. Fay, Philadelphia.—p. 221.

Public Health Reports, Washington, D. C.

57:1883-1922 (Dec. 11) 1942

Lesions in Rats Given Sulfaguanidine in Purified Diets. L. L. Ashburn, F. S. Daft, K. M. Endicott and W. H. Sebrell.—p. 1883.
Transmission of Plasmodium Lophurae, Avian Malaria Parasite, by Anopheles Quadrimaculatus. H. S. Hurlbut and R. Hewitt.—p. 1891.
Sulfanilamide in Treatment of Leprosy. G. H. Faget, F. A. Johansen and Hilary Ross.—p. 1892.
Antibacterial Action of Several Sulfonamide Compounds on Hemophilus Influenzae Type B. Margaret Pittman.—p. 1899.

57:1923-1962 (Dec. 18) 1942

Experimental Chemotherapy of Burns and Shock: I. Methods: II. Effects of Local Therapy on Mortality from Shock. S. M. Rosenthal.—p. 1923.
Observations on Epidemiology of Leprosy. G. W. McCoy.—p. 1935.
Location and Movement of Physicians, 1923 and 1938—Effect of Local Factors on Location. J. W. Mountin, E. H. Pennell and Virginia Nicolay.—p. 1945.

Rocky Mountain Medical Journal, Denver

40:1-72 (Jan.) 1943

Reaction of Central Nervous System to Trauma. W. M. Craig, Rochester, Minn.—p. 18.
Cardiac Irregularities and Tachycardias. J. G. Carr, Chicago.—p. 27.
Treatment of Fractures of Upper End of Humerus. G. A. Caldwell, New Orleans.—p. 33.
Progress in Burn Therapy. D. W. Macomber, Denver.—p. 34.

South Carolina Medical Assn. Journal, Florence

38:307-344 (Dec.) 1942

Recent Advances in Chemotherapy. W. H. Barker, Baltimore.—p. 307.
*Metrazol (Pentamethylenetetrazol) in Auricular Paroxysmal Tachycardia. W. W. Boyd, Spartanburg.—p. 317.
Functional Heart Disease. H. Smith, Greenville.—p. 318.

Metrazol in Auricular Paroxysmal Tachycardia.—Boyd tried unsuccessfully all the recognized procedures and drugs to abort a prolonged paroxysm of tachycardia. He gave 1½ grains (0.1 Gm.) of metrazol intravenously and noted almost immediate improvement in the patient's general condition. The attack ceased within two or three minutes. He has used the drug for 11 patients who did not respond to vagovagal stimulation, with almost immediate relief in all but 1. This patient responded to an intravenous dose of 12 grains (0.8 Gm.) of digitalis. The response in these patients and those of other physicians may have been coincidental, but the author believes it is due to the action of the drug, since the response has been uniform in all.

Southern Medical Journal, Birmingham, Ala.

36:1-86 (Jan.) 1943

Progress Against Bacillary Dysenteries. H. Emerson, New York.—p. 1.
Accelerated Program in Medical Schools. F. H. Swett, Durham, N. C.—p. 5.
Recent Advances in Study of Cancer. J. S. Horsley, Richmond, Va.—p. 8.
Modern Interpretation of Physical Therapy. F. H. Ewerhardt, St. Louis.—p. 12.
Compensatory Divergent Strabismus. C. A. Clapp, Baltimore.—p. 15.
Some Observations on Maxillary Sinus. L. C. McHenry, Oklahoma City.—p. 18.
Premenstrual Cystitis. L. A. LeDoux, New Orleans.—p. 22.
Vaginal Biopsy Studies After Total Hysterectomy. W. O. Johnson, Louisville, Ky.—p. 23.
Postoperative Management of Anal Surgery. G. F. Eubanks, Atlanta, Ga.—p. 29.
Patient After Gastric Surgery. D. C. Browne and G. McHardy, New Orleans.—p. 32.
Obstetric Problems in the Rural South. R. E. Seibels, Columbia, S. C.—p. 41.
Effect of Diabetes on Nervous System. W. R. Jordan, Richmond, Va.—p. 45.
Psychotherapy. G. F. Witt, Dallas, Texas.—p. 49.
Consideration of Factors in Therapy of Dermatitis. T. W. Murrell, Richmond, Va.—p. 50.
Old Wine in New Bottles. G. W. Leadbetter, Washington, D. C.—p. 52.
Pediculosis Capitis Treatment Among School Children in District of Columbia. J. A. Murphy, Washington, D. C.—p. 53.

Southern Surgeon, Atlanta, Ga.

11:809-878 (Dec.) 1942

*Chemical Transformation of Iodine Fixed by Thyroid Gland. W. Mann and C. P. Leblond, Rochester, N. Y.—p. 828.
Repair of Cranial Defect by Insertion of Vitallium Plate. W. H. Parsons, Vicksburg, Miss.—p. 840.
Spondylolisthesis Treated by Posterior Bone Graft: Fracture of Vertebra Above Graft. H. A. Swart, Charleston, W. Va.—p. 846.
Intravenous Anesthesia in Major Surgery (Sodium Pentothal Oxygen). T. C. Davison, Atlanta, Ga.—p. 849.
Infected Presacral Dermoid Cyst with Perforation of Vagina. G. H. Ewell and R. Jackson, Madison, Wis.—p. 855.
Surgical Management of Certain Phases of Lesions of Stomach and Duodenum. C. J. Hunt, Kansas City, Mo.—p. 859.

Transformation of Iodine Fixed by Thyroid Gland.—The fate of the iodine in the thyroid was determined by Mann and Leblond in two groups of dogs: those given amounts of iodine comparable to the minute quantities present in the food of man and those receiving a dose of iodine comparable to that used in therapy. In physiologic conditions the iodide coming from the blood stream accumulates in the thyroid mainly as diiodotyrosine. This is the natural precursor of thyroxine. The results indicate that 1.55 per cent of the thyroxine contained in the thyroid is formed hourly. When excessive or therapeutic doses of iodine are administered, the iodine is incorporated in the gland probably as stored iodide. In relation to the large dose administered, the proportion which is transformed into diiodotyrosine is much smaller than in the small dose administration.

Southwestern Medicine, Phoenix, Ariz.

26:407-428 (Dec.) 1942

Tumors of Testis. M. L. Day, Phoenix, Ariz.—p. 408.
Simplified Tourniquet for Venipuncture. W. M. Hayes, Hamilton, Ohio.—p. 411.
Some Considerations of Water Balance in Health and Disease. C. N. Ploussard, Phoenix, Ariz.—p. 412.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

26:529-576 (Dec.) 1942

Traumatic Ulcer of Cornea, with Special Reference to Coal Miners. R. M. Dickson.—p. 529.
Sympathetic Ophthalmitis. T. H. Butler.—p. 546.
Choroidal Melanoma Treated by Surgical Diathermy. L. H. Savin and G. C. Pritchard.—p. 551.
Test Type. J. P. S. Walker.—p. 556.

British Journal of Tuberculosis, London

36:153-188 (Oct.) 1942

Malignant Adenomatosis (Alveolar Cell Tumor) of Lung. J. V. Dacie and C. Hoyle.—p. 158.
Hematogenous Malignant Deposits in Lung Simulating Tuberculosis. G. S. Erwin and H. G. H. Butcher.—p. 166.
Bronchial Carcinoma with Infiltration of Left Auricle of Heart. B. A. Dormer, J. Friedlander and F. J. Wiles.—p. 169.
Hemoptysis: Case. N. R. Barrett and C. Hoyle.—p. 172.
Chronic Miliary Tuberculosis: Case Report. P. Hutchison.—p. 177.

Journal of Laryngology and Otology, London

57:401-426 (Sept.) 1942

Headaches of Acute Nasal Sinusitis and Attempt to Explain Them. E. Wodak.—p. 401.
Periosteal Flap in Mastoid Surgery. W. O. Reid.—p. 405.

Lancet, London

2:633-660 (Nov. 28) 1942

Chemistry and Physics of Antiseptics in Relation to Mode of Action. A. Albert.—p. 633.
*Dyspepsia in the Royal Navy: Study of 1,003 Consecutive Cases. H. J. Wade.—p. 636.
Radiologic Evidence of Decalcification in South Africa. A. A. Meyer, S. F. Oosthuizen and H. A. Shapiro.—p. 639.
*Passive Hyperemia for Chilblains. H. Herxheimer.—p. 640.
Unusual Meningococcic Relapse Syndrome. A. B. Christie.—p. 641.
Diphtheria Immunization in England and Wales: Statistical Study of Reactions and Difficulties of Mothers. Committee for the Study of Social Medicine.—p. 642.

Dyspepsia in the Royal Navy.—Wade states that 217 of the 1,003 consecutive cases of dyspepsia encountered at a large navy auxiliary hospital between October 1939 and October 1941 were in the active service of the Royal Navy and 786 were reserve and "hostilities only" personnel. The diagnosis in all was confirmed by roentgen examination or at operation. There is no evidence that wartime service in the Royal Navy has increased the incidence of dyspepsia. The expansion of the service and the inclusion of personnel from the prewar civilian population account for any apparent increase in incidence. An urgent need for organized clinical research into all aspects of the problem of dyspepsia of uncertain origin (so-called gastritis) is revealed; in the series such dyspepsia was diagnosed in 24 per cent of the patients, 175 of whom had joined the service since the war began. Usually the history was long; only 12 per cent of the patients with duodenal ulcer and 20 per cent of those with duodenal dyspepsia dated their symptoms from the taking up of war service; 62 of 404 with duodenal ulcer and 17 of 148 with duodenal dyspepsia had symptoms for eleven to fifteen years. Of the 1,003 patients 56 per cent had clinical ulcers, in 47 per cent ulceration was proved roentgenologically (6.7 per cent gastric, 40 per cent duodenal and 0.5 per cent anastomotic), 15 per cent had duodenal dyspepsia and 24 per cent suffered from dyspepsia of uncertain origin. Patients with proved peptic ulceration should be invalided from the service unless circumstances permit adequate dietary control. In all, 329 of the 1,003 were invalided from the service. Overcooking, reheating of meals, excess of canned and fried food and short mealtime are difficult factors to control on small ships. Many patients had taken alkaline powders regularly to control symptoms.

Passive Hyperemia for Chilblains.—Herxheimer produced artificial hyperemia by Bier's method of applying a constricting rubber bandage at the middle of the humerus or femur of 24 persons suffering from chilblains. Most of the patients were schoolboys; the treatment of 21 was completely successful in five to seven days: swelling, pain and itching disappeared and small ulcers and cracks of the skin healed. The only remaining sign was redness of the skin, sometimes associated with thickening and wrinkling. In spite of this early success, treatment was continued for at least six weeks because if it was interrupted after a week or a fortnight the chilblains recurred at once but did not after the prolonged period of treatment. A Martin's bandage 2½ to 3 inches wide was used, but any other elastic bandage, even bandages made without rubber, will do. The color of the limb should deepen under its influence, but it should not become colder to the touch than it was before, and the feeling of pins and needles should not ensue. On the other hand, the constriction should be so firm that this sensation and coldness are only just avoided. A reliable sign of correct technic is that the big veins in the elbow protrude and that the arm is deep purple without being uncomfortable. In some cases swelling of the hand, a sign of too firm bandaging, is visible next morning, but this subsides in a few hours. The bandage may be left in position for twenty-two out of the twenty-four hours, but usually all night treatment is sufficient. The beneficial effect of this local venous congestion is not easily understood. It seems that the unhindered arterial inflow forces blood through all potential blood spaces in the limb, including the capillary spaces dilated (and paralyzed) by cold, thus reopening the circulation through them.

Medical Journal of Australia, Sydney

2:433-454 (Nov. 14) 1942

Remarks on Some Fundamental Principles in Otorhinolaryngology of Interest in General Practice. B. Hiller.—p. 433.
Blood Grouping of Aborigines of Northwest Australia. R. K. Gay.—p. 435.

2:455-474 (Nov. 21) 1942

Arms and Anophelines, or Military Significance of Malaria. R. Fowler, with addendum by A. H. Baldwin.—p. 455.
Treatment of the Wounded in Forward Areas. E. W. Kyle.—p. 459.
Physical Signs of Pleural Collection, with Particular Regard to New Sign for Its Detection. M. Berah.—p. 463.

Practitioner, London

149:321-384 (Dec.) 1942

Industrial Medicine and the General Practitioner. D. Munro.—p. 321
Chest Disease in Industry. A. J. Amor.—p. 326.
Industrial Dermatitis: Diagnosis and Treatment. A. D. K. Peters.—p. 340.
Treatment of the Injured Workman. W. Gissane.—p. 349.
Problems of Neuroses in Industry. E. H. Capel.—p. 354.
Advances in Treatment of Chronic Nasal Sinusitis. J. Harper.—p. 364.
Minor Surgery: Anesthesia and Analgesia. C. L. Hewer.—p. 373.

Quarterly Journal of Medicine, Oxford

11:181-246 (Oct.) 1942

*Pathologic Changes in Brain in Fatal Hypoglycemia. R. D. Lawrence, A. Meyer and S. Nevin.—p. 181.
Maffucci's Syndrome (Dsychondroplasia with Hemangiomas). Alice Carleton, J. St. C. Elkington, J. G. Greenfield and A. H. T. Robb-Smith.—p. 203.
Localized Pretibial Myxedema in Association with Toxic Goiter. W. R. Trotter and K. C. Eden.—p. 229.

Changes in Brain in Fatal Hypoglycemia.—The neuropathologic changes in 6 fatal cases of hypoglycemia are described by Lawrence and his associates. The lesions were similar in all and differed only in intensity and the stage of the process. Widespread degeneration and necrosis of nerve cells were found, with corresponding microglial and macroglial proliferation; homogenizing and severe nerve cell changes were the predominating types of degeneration. The cerebral cortex, the caudate nucleus and the putamen were most affected, the cerebellum less so and the remaining centers of the brain stem were slightly involved. In 2 cases a widespread glial fibrosis of the cerebral and cerebellar white matter was a striking feature. The pathogenesis is discussed in relation to the biochemical alterations in hypoglycemia and in comparison with similar lesions in anoxia. The main cause is considered to be failure of the vital oxidative processes from lack of substrate dextrose, probably reinforced by subsequent vasomotor disturbances. The primary factor seems to be chemical and akin to anoxia.

Ophthalmologica, Basel

104:121-176 (Sept.) 1942

Problem of the Weil-Felix Reaction in Trachoma. L. Poleff—p. 121.
*Ocular Inflammations of Focal Origin. D. Anastassoff.—p. 136.
Differential Perception for Brightness of Eyes Adapted to Darkness. G. B. Saubermann.—p. 157.
Production of Aqueous Humor and Development of Glaucoma. P. Weinstein.—p. 166.
Instrument to Facilitate Suture of Mucosa in Dacryocystorhinostomy. A. Bangerter.—p. 171.

Ocular Inflammations of Focal Origin. — Anastassoff reports 6 cases of iridocyclitis of which 4 had their origin in an infected dental root, 1 in the tonsils and 1 in the prostate. In 2 cases of episcleritis a focus of infection existed in the tonsils. By means of Rosenow's technic Anastassoff was able to produce an iridocyclitis in rabbits and an immature cataract. Bacteriologic examination disclosed no specific agent, leading the author to conclude that the lesions were of a toxic nature.

Schweizerische medizinische Wochenschrift, Basel

72:833-856 (Aug. 1) 1942

Nature and Treatment of Bronchial Asthma. O. Müller.—p. 833.
Study of Case of Chronic Bacteremia and Question of Its Place in Nosology of Tuberculosis. R. Burnand.—p. 838.
Unusual Roentgen Findings in Region of Digestive Tract. H. Gysin. —p. 841.
*Nystagmus as Recessive Sex Linked Characteristic in Four Generations. O. Käser.—p. 846.
*Wound Treatment with Chlorophyll Ointment. F. Boehringer.—p. 850.

Nystagmus as Recessive Sex Linked Characteristic.—Käser presents the genealogical table of a family with hereditary nystagmus. The table includes six generations and 121 persons, of whom 13, or 10.7 per cent, had a pronounced nystagmus. The pronounced nystagmus appeared only in men but was transmitted by women. Thus it is a recessive sex linked defect. In addition to the 13 persons with pronounced nystagmus 3 men and 3 women were discovered with a nystagmus elicited only on extreme rotation. One man exhibited jerking of the head without accompanying nystagmus. Nystagmus on extreme rotation and jerking of the head in supposedly healthy members of the family are interpreted as manifestations of a familial defect. Three persons presented nystagmus and head jerking in combination. The family likewise included members with amblyopia, myopia, hypermetropia and astigmatism, but also many with normal eyes.

Wound Treatment with Chlorophyll Ointment.—At Boehringer's clinic in Bern, it is the rule to test new remedies for wounds only when control experiments can be made, as on patients with several wounds or a single wound of such extent as to permit one half to be treated with the new preparation and the other with a control substance. Under such conditions the differences in results with the use of expensive ointments and isotonic solution of sodium chloride were negligible. In some instances isotonic solution of sodium chloride actually appeared superior. Chlorophyll ointment has been tested at the Bern clinic for some time. Of the 8 cases in which chlorophyll ointment was used and in which other salves were employed for control purposes, 7 exhibited better granulation under chlorophyll ointment than under that of other ointments. Epithelial growth was the same under chlorophyll and control ointments. One case failed to respond to ointment treatment of any kind. In 5 additional cases treatment with chlorophyll ointment produced a favorable change in chronic torpid wounds. Chlorophyll ointment has proved particularly valuable in torpid wounds and in wounds with extensive and deep tissue defects.

Revista Médica Cubana, Havana

53:649-744 (Aug.) 1942. **Partial Index**

*Surgical Therapy of Ozena. C. de Lejarza.—p. 670.
Diagnosis and Therapy of Tumors of the Bladder. R. Portilla.—p. 689.

Surgical Therapy of Ozena.—De Lejarza states that the caliber of the nasal fossae is greatly enlarged in ozena. There is a general belief that the amplitude of the nasal fossae and the consequent local increased ventilation are the causal factors of the condition and that it can be improved by any surgical operation which reduces the size of the fossae. The author reports the case of a girl aged 24 with typical ozena. There was no infection of the maxillary sinuses. The therapy of ozena in this case consisted in opening the maxillary sinuses by a surgical operation and leaving them open. The patient recovered.

Rev. Méd.-Quirúrg. de Pat. Femen., Buenos Aires

20:145-224 (Sept.) 1942. **Partial Index**

New Apparatus for Extracting Estrogens and Androgens from Urine. A. E. Raices.—p. 145.
*Preserved Blood. A. Battaglia.—p. 151.
*Estrogen Therapy of Retention of Urine in Postoperative Period of Extensive Pelvic Interventions. F. Bazterrica and J. A. Poch.—p. 186.

Conserved Blood.—Battaglia believes that conserved blood is indicated only in emergencies when fresh blood is not available. In the Department for Blood Transfusion of the Hospital Rivadavia, 1,500 transfusions have been performed in the last four years. Conserved citrated blood was used in 181 transfusions. The amount varied from 50 to 550 cc. for a transfusion. Blood conserved for less than a week was used in 153 transfusions. Blood conserved for thirty-one days and forty-four days respectively was used in only 2 cases. Conserved citrated blood is tolerated better than fresh blood. Conserved blood which shows evidence of early hemolysis due to shaking of the flasks is also well tolerated. Transfusion of conserved blood does not cause hemoglobinuria or symptoms of renal damage. Best results are obtained from blood conserved for not more than three days. Fresh blood is indicated in acute and chronic infection, anemia, shock and hemorrhage. If fresh blood is not available, conserved blood not older than 3 days can be used.

Estrogen Therapy of Urinary Retention.—Bazterrica and Poch's patient with extensive rectovaginal cancer was subjected to abdominoperineal resection of the rectum and hysterectomy. The ensuing shock was combated by transfusion, intravenous dextrose and cardiac tonics. Intractable retention of urine established itself from the first postoperative day. A permanent catheter was kept for thirty-five days. Intramuscular injections of estrogens in doses of 60,000 units given at intervals of three and four days respectively up to a total of six injections rapidly controlled the retention.

Revista Peruana de Pediatría, Lima

1:1-146 (Sept.) 1942

*Cholesteremia in Healthy Infants and Its Variations in Dystrophy and Toxicosis. G. Llosa Ricketts.—p. 1.
Case of Still's Disease. L. A. Suares.—p. 25.
Tuberculosis in Children of Lima. H. Cachay Diaz.—p. 44.
Universal Blood Donors. T. Escajadillo.—p. 56.
Osteoarticular Tuberculosis in Infancy. R. F. Tijero.—p. 65.

Cholesteremia in Healthy Infants and in Dystrophy and Toxicosis.—According to Llosa Ricketts the biologic role of cholesterol in immunity, in erythrocytic resistance, in cellular absorption and as an antitoxic factor has acquired great importance in the light of recent studies. There is no record of the importance of cholesterol in dystrophy and toxicosis. The author investigated blood cholesterol by means of an electric photocolorimeter in young children with these two disorders. His studies were made on 57 infants and children: 15 were healthy, 22 had dystrophy and 20 had toxicosis. The quantity of cholesterol in healthy children up to 2 years of age averaged 171 mg. per hundred cubic centimeters and varied between 140 and 200 mg. There exists a close parallelism between the weight and the cholesterol content of the blood. In obese children the blood cholesterol values may reach 250 mg. per hundren cubic centimeters. Dystrophy is always accompanied by hypochlolesteremia, which is the more pronounced the more grave the dystrophy. The lowest values, 53, correspond to athrepsia. The blood cholesterol content of children with toxicosis is likewise inferior to the normal average; it decreases in direct ratio with the loss of water. One of the factors responsible for infection, anemia, disturbance in water exchange and the toxic state, which are observed in dystrophy and toxicosis, is hypocholesteremia. The determination of the quantity of blood cholesterol ip dystrophy and toxicosis is of prognostic importance. The prognosis is unfavorable when values of less than 100 mg. per hundred cubic centimeters are present.

Book Notices

Therapeutics of Infancy and Childhood. Edited by Harry R. Litchfield, M.D., F.A.C.P., Attending Pediatrician, Beth-El Hospital, Brooklyn, and Leon H. Dembo, M.D., Visiting Pediatrician, St. Luke's and St. Anne's Hospitals, Cleveland, Ohio. [With] 117 Contributors. In four volumes and desk index. Fabrikoid. Price, $32. Pp. 816; 1001-1816; 2001-2745; 3001-3831; 1-203, with illustrations. Philadelphia: F. A. Davis Company, 1942.

One hundred and seventeen contributors have combined to prepare this work, which includes four volumes and a desk index. Forty years have passed since the publication of Jacobi's comprehensive book on the therapy of infancy and childhood. The advances that have been made since that time, particularly in relationship to specific therapy, biologic and glandular therapy and new methods of treatment for diseases formerly considered incurable would alone warrant a work of such great scope as is the system here reviewed. Moreover, the mental aspects of child care are in themselves so important and have been so exhaustively investigated that they too would well warrant a systematic discussion.

Recognition of the importance of the mental aspect is revealed in the first chapter, which is concerned with the psychologic care of the sick child, followed by another on the art of treatment. Then come considerations of legislation affecting therapy, medical aid until the doctor comes, and a consideration of various materials and technics used in treatment. The remainder of the first volume is devoted to asphyxia neonatorum, anomalies, nutrition, disorders of the skin and the acute infectious diseases.

Subsequent volumes cover rheumatic fever, the diseases of various regions of the body including the circulation, diseases of metabolism and of the nervous system; and, in the final volume, tropical diseases, radiation therapy, diseases of the skin and surgery. A detailed index volume completes the work.

The selection of authors has been excellent, embracing most of the well known pediatric clinics of the United States. The type selected is an exceedingly large type with plenty of white space, indicating no doubt the development and planning of this work well in advance of the restrictions now placed on paper and printing by the exigencies of the war. The modern character of the work is shown in the special chapter on blood plasma, which is discussed in great detail with numerous illustrations. Indeed, the many colored illustrations in this work are an indication of its comprehensive and elaborate approach to this subject.

In his chapter on whooping cough Dr. Sauer has brought down to date the present point of view regarding that disease. Each of the chapters is accompanied by a bibliography, unfortunately limited to names of authors and periodical references without in any instance providing titles of the articles concerned. For the young man about to undertake a pediatric practice, a work of this type is exceedingly valuable since it will bring him promptly into touch with the latest points of view regarding any of the problems which may come before him. As might be expected in such subjects as the treatment of burns and in much of the surgery concerned, time was too short to permit some of the changing points of view brought about by the experience of the war. It is rather strange to find appended to the volume, almost as an afterthought, a special chapter on hypertension—a subject which, incidentally, is not of primary importance as a condition affecting the child.

The Hormones in Human Reproduction. By George W. Corner. Cloth. Price, $2.75. Pp. 265, with 56 illustrations. Princeton, New Jersey: Princeton University Press; London: Oxford University Press, 1942.

The author presents a comprehensive story of reproduction, beginning with the simple processes exhibited in the lower animals and ending with the complicated processes in the higher apes and the human being. The physiology of menstruation, ovulation, fertilization and early implantation of the fertilized ovum are clearly described. The changes in the uterus and the endocrine glands as a result of pregnancy are discussed. Most of the chapters are devoted to the glands and the hormones which control reproduction. The discovery of the ovarian hormones, their isolation, their chemistry and their physiologic role are described by presenting many key experiments by numerous investigators. The story of progesterone, with which the author was closely identified, is particularly interesting.

This small monograph is the result of the Vanuxem Lectures which the author delivered at Princeton in February 1942. These lectures with many additions have been embodied in one of the most delightful books that has come to the attention of the reviewer in many years. All the scientific data have been carefully evaluated by one of the foremost scholars in the field of reproduction and yet they are presented in such a simple, interesting manner that any college student can follow the discussion with ease. The numerous illustrations, many of which are simple, add greatly to the clarity and interest of the text. Pertinent quotations from the literature introduce each chapter. This small book should be read by every student of biology as well as by the ever increasing number of men and women who are intrigued by the miracle of reproduction.

Just for Two: A Handbook of Cookery for the Small Household. By Lily Haxworth Wallace. Cloth. Price, $2. Pp. 311. New York: M. Barrows & Company, Inc., 1942.

Home Canning for Victory, Also Preserving, Pickling and Dehydrating. Compiled and edited by Anne Pierce. Cloth. Price, $1.25. Pp. 166, with 3 illustrations. New York: M. Barrows & Company, 1942.

Diet Without Despair. By Marion White. Cloth. Price, $1.50. Pp. 128. New York: M. S. Mill Co., Inc., 1943.

Sweets Without Sugar. By Marion White. Sixth printing. Cloth. Price, $1.25. Pp. 128. New York: M. S. Mill Co., Inc., 1943.

The Food You Eat: A Practical Guide to Home Nutrition. By Samuel and Violette Glasstone. Cloth. Price, $2.25. Pp. 277, with 18 illustrations. Norman: University of Oklahoma Press, 1943.

If ever anybody needs a cookbook, it is likely to be the new bride who is trying to plan meals for herself and her husband. Even her mother will sometimes have trouble translating the quantities of a large household into something suitable for two people. There are many dishes that are easy to make and are economical when prepared for a large family but difficult, if not impossible, to prepare in small amounts. "Just for Two" is designed particularly for meeting this need. It begins with a statement on the essentials of a well balanced diet, indicates the need for a satisfactory breakfast and lunch, particularly for those who are working, and then provides innumerable recipes worked out in chapters according to the class of foods concerned. Sections on how to market and how to plan daily meals for variety, flavor, nutrition value and economy are especially worth while.

The experience of the author of "Home Canning for Victory" in conducting the section of the New York *Herald-Tribune* concerned with home economics is warrant of her ability to consider the subject which she covers in this book. All of the problems related to home canning are modified at this time by the ability to secure materials to be canned and packages in which to do the packing. Dehydration is for most people a new process. Miss Pierce considers home canning, preserving, making pickles and relishes and dehydration of food. A number of articles in the appendix are especially practical. Here are time tables for all of the processes involved and a discussion of utensils and of the sugar situation. The book is excellently printed.

Dieting demands, most of all, will power and full information regarding the number of calories in an ordinary serving of most foods. "Diet Without Despair" provides the charts and, in addition, a good many recipes for items that are low in calories. There is even a section devoted to cakes and pies, with the warning that the butter and the cream and sugar in the frosting are the chief items to be avoided. Here is information on how to make a low calory sponge cake and also menus for such special occasions as bridge luncheons, afternoon teas, midnight snacks and drugstore luncheons for the business girl. By its emphasis on mathematics this book fills a special need.

Miss White has also made available a book on "Sweets Without Sugar" and, for that matter, without saccharin. She substitutes, however, honey, molasses, corn syrup and maple syrup, with a recognition of their content. Unfortunately, some of the statements regarding the food value of the substitutes are slightly exaggerated, since they do not take account of the amounts of these substances necessary to give equal sweetening value.

The university presses are making many valuable contributions to American publications. "The Food You Eat" from the University of Oklahoma is a modern, up-to-date, simple presentation of food problems based on a knowledge of the physiology of digestion, new information regarding the vitamins and a practical experience with menus. The book is supplemented with an outline on practical nutrition and a good index.

Abdominal and Genito-Urinary Injuries. Prepared under the Auspices of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Abdominal Injuries: Prepared by Ambrose H. Storck. Evarts A. Graham, Chairman. Genito-Urinary Injuries: Prepared and edited by the Subcommittee on Urology of the Committee on Surgery. Herman L. Kretschmer, Chairman. Volume III. Military Surgical Manuals. Cloth. Price, $3. Pp. 243, with 79 illustrations. Philadelphia & London: W. B. Saunders Company, 1942.

This is the third volume of a series of six manuals prepared under the auspices of the Committee on Surgery of the National Research Council as concise presentations of fundamental knowledge in the various fields of surgical specialization in relation to military surgery. They were originated, planned and largely written before Pearl Harbor, being thus a monument to the foresight of the surgical profession but perhaps suffering slightly from their prewar origins. The set of war manuals was designed to crystallize in short, practical form present day knowledge of the basic principles of surgery in all fields of specialization, applied to the problems of trauma produced by enemy action. The volume under review is well done and will probably suffer little from new observations based on experience on the firing lines of today.

Part I, on abdominal injuries, comprises eleven chapters with many pertinent and well executed drawings by Miss Vera Morel that illuminate and clarify the text. The chapters deal in an orderly manner with all phases of the management of abdominal injuries from their reception, study and diagnosis to general care and preoperative preparation, the selection for operation, the anesthetic, the operative procedure, wounds of special organs, postoperative treatment, complications and a final evolution of results, mortality and statistics. The whole is covered by an emphasis on the patient rather than on one particular injury, with excellent balance and an emphasis on fundamentals that will not change although they may be garnished by newer experience in the field. There is at this time no more pithy presentation of the basic principles of the treatment of abdominal trauma than is here proffered, and the author is to be heartily commended for an admirable summary of postwar experience, combined with modern scientific advances.

Part II consists of six chapters on genitourinary injuries, prepared and edited by a distinguished group of urologists, and is comprehensive, authoritative and complete. Diagnostic methods are explained in great detail and in a practical way. The discussion of renal and ureteral injuries is commendable for its completeness and soundness. The treatment of crushing injury and renal failure is both timely and apropos. However, in light of recent research it is becoming evident that, in cases reported in the British literature, renal failure has not resulted from toxic degenerative products of traumatized muscle, as has been thought by the foreign observers, but rather from intravenous saline solution administered to these patients for treatment of their shock. The complete discussion of the care of the neurogenic bladder is particularly praiseworthy and should be read and reread by all physicians who expect to treat war casualties. The principles enunciated are sound, and the procedures described are essential to good practice in this difficult group of cases.

This volume can be heartily recommended to those who will have opportunity for treating patients injured by missiles of war and accidents of civil life.

The Standard of Living in 1860: American Consumption Levels on the Eve of the Civil War. By Edgar W. Martin. Cloth. Price, $4.50. Pp. 451. Chicago: The University of Chicago Press; London: The Cambridge University Press, 1942.

A distinguished committee which studied economic changes in the United States in 1923 pointed out that the most significant factor in the changes that had occurred in the previous quarter century had been the increasing expansion of human desires and wants. In no other field perhaps has this expansion been more significant than in the field of medicine and public health. The author discusses the conditions that prevailed in 1860 in diets, housing, clothing, transportation, education and leisure. One chapter is devoted to medical care and the public health. Characteristic of the 50's were high death rates and low life expectancy. The first disease microbe was identified in 1863, but anesthetics had come in in 1844. Quacks and frauds preyed on the ignorant masses; phrenologists and spiritualists claimed special abilities; hydropathy and homeopathy were in their heydey. The legal requirements for practice were not exacting. There were only faint indications of trends toward specialization. At that time there were only 5,600 dentists in the country, or about 18 for every 100,000 persons. There were only 8,000 nurses, or about 26 for every 100,000 persons. The first hospital training school for nurses was opened in 1873. As late as 1890 there were less than 500 graduate nurses in the United States. There were wide differences between the quality of medical practice in different parts of the country. In many plantations physicians were employed on a yearly salary to take care of slaves. The average annual income for country doctors in Alabama was $1,000; $2,000 for the city practitioner. Medicine was then just on the threshhold of becoming a science. In 1873 there were only 149 hospitals in the country; in 1923 there were 6,762. In the Massachusetts General Hospital at that time there was no attempt to classify or segregate patients. There was no public health nursing until 1877. Only a few cities had boards of health in 1860. The first state board of health was established in 1869. From a recapitulation of the situation then prevailing and a comparison with the advancements of today one must derive great encouragement.

Diseases of Women. By Ten Teachers under the direction of Clifford White, M.D., B.S., F.R.C.P. Edited by Sir Comyns Berkeley, Clifford White and Frank Cook. Seventh edition. Cloth. Price, $6. Pp. 435, with 168 illustrations. Baltimore: William Wood & Company, 1942.

It is a remarkable achievement to revise a book under present conditions existing in Great Britain. That this has been successfully accomplished by nine contributors is even more creditable. The popularity of this gynecologic textbook is evidenced by the fact that this is the seventh revision. The gynecologic subjects are covered in a brief and concise manner, including the etiology, symptoms, diagnosis and treatment. Controversial data have been entirely eliminated. All the contributors have read and constructively criticized the entire book, so that the conclusions represent a good cross section of gynecologic thought and practice in the British Isles. There is little to which one can take exception. The Wertheim operation for carcinoma of the cervix has been replaced by irradiation in most clinics in the United States. American gynecologists do not favor the transplantation of ovarian fragments in the event that it is necessary to remove both ovaries in young women. A few operative procedures are presented rather sketchily in the last chapter. The descriptions may be sufficient for one who has had operative experience but they would not suffice for the novice. The book is an excellent outline of gynecologic thought and practice.

Silent Enemies: The Story of the Diseases of War and Their Control. By Justina Hill. Cloth. Price, $2.50. Pp. 266. New York: G. P. Putnam's Sons, 1942.

The success of Dr. Hill's contribution "Germs and the Man" has led her to reflect for the public interest some of those conditions caused by bacteria which are particularly a problem of war. Thus she has sections on the tropical diseases, the plagues, wounds and burns, the respiratory diseases, filth, venereal diseases and the viruses. The final chapter indicates the tremendous scope of the postwar problem, which involves the freeing of the world from the menace of all the various forms of contagion likely to become widespread by the movement of great bodies of troops. The health problems of relief and reconstruction abroad, including the care of refugees, are likely to be almost as difficult a task as the winning of the war itself. Badly needed, says Dr. Hill, is a chemical coup for the viruses equivalent to what the sulfonamides have done for the bacteria. Needed also are drugs of equal potency against tuberculosis and syphilis. She indicates the need for improved research in many fields. Altogether, the book is one of the most pleasantly written and informative available to the general reader.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

HYPERHIDROSIS OF FEET

To the Editor:—**A man aged 27, a butcher, shows no physical abnormalities but he presents an unusual and, to him, a distressing phenomenon. In summer his body perspires profusely, yet his feet are dry; in the winter the reverse is true, his body being dry but his feet constantly wet with perspiration, even though he bathes his feet daily, wears thin socks and shoes, and does the same amount of work the year round. Please advise me regarding the probable cause of this condition and what can be done for it.**

M.D., New York.

ANSWER.—The general sweating of the body in the summer is not remarkable, some people naturally sweating more than others. This may be increased by such diverse factors as obesity, hyperthyroidism, organic changes in the central nervous system and exhausting illness. The hyperhidrosis of the soles would not be expected to manifest itself particularly in summer, because the sweating of the palms and soles is somewhat independent of temperature. At these sites accentuation is speeded up by emotional stress. Here too the insensible perspiration is greater than at other sites, except perhaps at the axillas. This insensible perspiration consists of two elements, namely the smaller amount as a physical discharge of water through the epidermis and the larger perpetual secretion of sweat. This not inconsiderable amount of liquid forming on the palms and soles regardless of temperature has to be volatilized. There might be a less ready evaporation during winter, especially in one whose skin is cool. At any rate persons with a chilblain type of circulation tend to have hyperhidrosis of the palms and soles. This is commonly expressed as the cold, clammy hand or foot. There are no data at hand to show whether such extremities actually sweat more or volatilize less readily what they do secrete by reason of lower surface temperatures. Other causes for hyperhidrosis of the soles may be flat feet and impaired circulation. It might be worth while inquiring into possibilities of undue stress or diet. It is known that certain articles of food and some drugs are capable of inducing excessive sweating in some people and especially at localized sites. Among such foods should be mentioned chocolate, tomatoes, cheese, pickles and onions.

If none of the elements suggested can be found in the background as contributing agents in this case, certain measures may be instituted to give some relief: Dehydration therapy with curtailment of the fluid intake and the administration of atropin or belladonna. For the feet, dusting powder of talcum or mixed with boric acid 5 to 10 per cent, salicylic acid 1 to 3 per cent and formaldehyde 1 to 3 per cent (formaldehyde is capable of producing a dermatitis through sensitization). Aqueous solutions of the following are somewhat easier to use and more effective: boric acid, salicylic acid or formaldehyde in 3 per cent concentration, aluminum chloride 10 to 25 per cent and sodium hexametaphosphate 1 to 5 per cent. They may be applied morning and evening and then less often when the amount of sweating is reduced. The use of x-rays for the control of hyperhidrosis is a method preferred by the patient. There is a difference of opinion regarding the advisability of its use. Conservative opinion holds that sufficient doses to produce atrophy are necessary to achieve the desired reduction in sweating. This in turn leads to persistent dryness of the palms and disagreeable sensations often worse than the original hyperhidrosis.

AMPHETAMINE FOR OBESITY

To the Editor:—**Kindly give me information as to the use of amphetamine (benzedrine) sulfate and dextroamphetamine in the treatment of obesity.**

M.D., California.

ANSWER.—Amphetamine sulfate is a sympathomimetic drug which stimulates the higher cerebral centers, especially the cortex. The dextrorotatory form is said to be two to four times more active than the levo form or dl mixture. Among its many actions it may cause anorexia with such associated complaints as nausea, belching, flatulence, abdominal cramps and a disturbance in bowel habits. Since anorexia follows its use, amphetamine has been employed in the treatment of obesity. It is maintained by Ersner that when a patient loses his appetite he is more likely to follow diet. With this statement there would be no disagreement.

The depression of the appetite would seem to be the chief action of amphetamine in the treatment of obesity, since the effect on the basal metabolic rate is neither constant nor significant. Altschule and Iglauer found an increase in the basal metabolic rate in only 2 of 12 normal subjects following the use of the drug, and in these they attributed the increase to restlessness. Dill, Johnson and Daly reported a definite calorigenic action following intramuscular injection in man.

The impression is gained that the loss of appetite, the increased activity and the restlessness of patients under the influence of amphetamine are sufficient to account for the weight loss which often follows its continuous use. This drug should be used only under the careful supervision of a physician, and when disagreeable side effects appear it should be discontinued.

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Dill, D. B.; Johnson, R. E., and Daly, Cornelius: Metabolic and Cardiovascular Effects of Intramuscular Injections of Adrenalin and Amphetamine, *Am. J. M. Sc.* **198:** 702 (Nov.) 1939.

EOSINOPHILIA AND PARASITIC INFECTION

To the Editor:—**I have recently had 2 patients with eosinophilia. The first, a man aged 61, a plumber, gave a history of becoming violently nauseated soon after eating a meal about Aug. 1, 1942. He does not remember what he ate. He had no diarrhea. About two weeks after this he began to tingle and itch all over his body from head to toes, and this tingling has continued to the present time. About the time the tingling began he had a severe itching spell and a red blotchy rash across the abdomen. He has lost 20 pounds (9 Kg.). He has not had further vomiting or muscle or joint pains. The physical examination was essentially negative. His blood picture on Dec. 4, 1942 was as follows: hemoglobin 90 per cent, erythrocytes 5,800,000, leukocytes 11,500, polymorphonuclears 29 per cent, eosinophils 53 per cent, lymphocytes 18 per cent. The sedimentation rate was 12 mm. in one hour. The serum Kahn and Kline reactions were negative. A biopsy from the deltoid muscle 5 mm. in diameter contained no trichinas. Examination of warm stools after a saline purge showed a few ova, both fertilized and unfertilized, of Ascaris lumbricoides. In the third stool passed were numerous parasites that fit the description of Strongyloides stercoralis, some of them alive and most containing ova. The other patient was a housewife aged 24. On Nov. 30, 1942, she complained of aching over the whole body but especially in the arms and of a severe headache. She had been aching for a week. The pain began in her right shoulder. Any movement starts the pain in the arm. There is no history of any gastrointestinal disturbance except cramping immediately after putting food in the stomach. There was no rash. Her temperature varied from 99.8 to 100.5 F. She gave a history of liking her meat not too well done and also of usually taking a bite of raw lean meat when slicing bacon. On Dec. 4, 1942 her blood picture was as follows: hemoglobin 75 per cent, erythrocytes 5,100,000, leukocytes 10,500, polymorphonuclears 59 per cent, eosinophils 21 per cent, lymphocytes 20 per cent. The sedimentation rate was 29 mm. in one hour. The serum Kahn and Kline reactions were negative. Muscle biopsy has been refused up to the present time. An examination of stools for parasites was done and no ova were found, but one parasitic worm was found containing a row of embryo worms. The embryos were partially uncoiled so that they formed a line of identical S's lying sideways. The head and tail of the adult worm were not seen. Neither of these patients has lived outside the state of Ohio. They have had no contact with each other. Intracutaneous tests with trichinella extract 1:10,000 were negative in the case of the man and a doubtful positive in the case of the woman. Could the first patient's symptoms be due to infestation with Strongyloides? What is the probable identity of the parasite found in the second patient?**

M.D., Ohio.

ANSWER.—In connection with the first case it is improbable that the symptoms and eosinophilia were due to Strongyloides. Only in extremely heavy infections is such a high eosinophilia encountered, and larvae would have been found in large numbers in every stool specimen. It is doubtful that the parasites found were Strongyloides because only larval forms would be found in fluid stools, and larvae do not contain ova. Parthenogenic female strongyloides would not be evacuated ordinarily by a saline purge. It is suggested that this patient's stools be examined again by a competent parasitologist. The eosinophilia might have been caused by sensitivity to some foreign protein other than an animal parasite. If the eosinophilia still persists, another cutaneous test for Trichinella might be performed, although the symptoms were not typical of that infection.

In the second case the description of the presence of an adult worm containing embryos is not typical of any parasite commonly infecting man. It might have been a free living worm swallowed with food or drink. The description sounds more like an artefact. In this case again a reexamination of the stools by a competent parasitologist is recommended.

TECHNICS OF ERYTHROCYTE SEDIMENTATION TESTS

To the Editor:—**I should like to ask regarding the present status of the normal range for the erythrocyte sedimentation index. During my internship and residency I used the Linzenmeier technic, wherein the time was recorded in which an 18 mm. fall occurred. This was two hours for women and slightly less for men, corresponding to 9 mm. an hour. This was frequently compared to the standard Wintrobe hematocrit tube. Yet in The Journal, March 7, 1942, page 779, the authors consider as an increased sedimentation rate one exceeding 20 mm. in one hour. My query is What is the normal index or rate for the various technics? Has any attempt at standardization of technics been made? How should the index be stated preferably, as time or as millimeters? Also it has been stated that pertussis, allergy and liver disease prolong the sedimentation time. Is it known in what way this occurs?**

R. G. Lehman, Lieutenant, M. C., U. S. N. R.

ANSWER.—There is no one standard method for performing the sedimentation rate, and the variety of technics and methods for expressing results continue to cause confusion. The Westergren method is probably used more than any other. In general the sedimentation rate of erythrocytes usually serves as a rough index of the concentration of plasma fibrinogen. The sedimentation rate of erythrocytes fails, however, as an index of plasma fibrinogen when there are abnormally elevated levels of serum globulins or of lipids and when there is advanced microcytic or macrocytic change in the red blood cells. The closest correlation between the sedimentation rate and the concentration of plasma fibrinogen has been obtained by use of the Rourke-Ernstene method and the Westergren method. Poorer correlation has been obtained by the methods of Linzenmeier, Cutler and Wintrobe-Landsberg. Each of these five methods, however, has proved useful clinically. The Rourke-Ernstene method is the most reliable but also the most time consuming and complex.

The Westergren technic is a simplified procedure which has been widely used and can be recommended since a single reading in millimeters taken at the end of one hour, uncorrected for anemia, has a high degree of correlation with concentration of plasma fibrinogen. This is true for the Westergren method performed as described by the author, employing 20 per cent by volume of 3.8 Gm. of sodium citrate solution per hundred cubic centimeters as an anticoagulant, mixed with 80 per cent by volume of venous blood, the mixture drawn into the Westergren tube. Other investigators have modified the proportion of sodium citrate solution used for the Westergren method or have substituted potassium oxalate as the anticoagulant. These modifications do not improve Westergren's method but add further confusion by changing the values for the normal and abnormal range of sedimentation rates. Change in the anticoagulant to a small volume potassium oxalate, for example, alters the characteristics of the settling velocity, increases the rate for normal subjects and increases the effect of anemia, which is minimal in the original Westergren method. The unmodified Westergren method performed with one reading at the end of one hour and without correction for anemia is the best simple method available for clinical purposes.

Preferably the sedimentation rate should be expressed as the number of millimeters of settling per hour or per minute as observed during the period of constant settling velocity rather than the less convenient method of Linzenmeier, namely the observation of the time in minutes required to settle 18 mm. A quantitative comparison of the five commonly used sedimentation methods has been reported by Ham and Curtis (*Medicine* **17**:413 and 447 [Dec.] 1938) and by Hambleton and Christianson: (*Am. J. M. Sc.* **198**:177 [Aug.] 1939). Ham and Curtis have also discussed the relation of plasma proteins, especially plasma fibrinogen and serum globulins, to the sedimentation rate. A table of normal and abnormal sedimentation rates is submitted here.

It has been reported that the sedimentation rate is prolonged in allergic states, certain virus infections and certain cases of brucella infection. This indicates that the concentrations of plasma fibrinogen and of serum globulins are not elevated in these diseases. In overwhelming liver disease, however, the sedimentation rate may decrease from an abnormally elevated level to normal, coincident with a decrease in the plasma fibrinogen from above normal to below normal, with resulting fibrinogenopenia. This is a sign of liver failure which is encountered rarely (Ham and Curtis, p. 413). A normal sedimentation rate or a so-called prolonged rate, therefore, is indirect evidence that

Comparison of Five Commonly Used Sedimentation Methods

	Rourke-Ernstene	Wintrobe-Landsberg	Westergren	Linzenmeier	Cutler
Sedimentation					
Tube length.....	120 mm.	120 mm.	300 mm.	65 mm.	70 mm.
Internal diameter..	4.0 mm.	2.5 mm.	2.5 mm.	5.0 mm.	5.0 mm.
Graduations.....	0-100 mm.	0-100 mm.	0-200 mm.	0-18 mm.	0-50 mm.
Height of blood column.....	100 mm.	100 mm.	200 mm.	50 mm.	50 mm.
Anticoagulant.....	Heparin, 15 per cent Dry oxalate mixture * Potassium oxalate †	Dry oxalate mixture *	Sodium citrate, 3.8 per cent	Sodium citrate, 5 per cent	Sodium citrate, 3 per cent
Amount.....	0.013 cc. heparin in 3 cc. blood. For oxalates see notes	See note	0.2 cc. in 1.0 cc. mixture	0.2 cc. in 1.0 cc. mixture	0.1 cc. in 1.0 cc. mixture
Concentration (mg. per 100 cc. mixture)	65 heparin 200 oxalates	200	760	1,000	300
Dilution of blood (per cent)	0.4 heparin 0.0 dry oxalate mixture 1.0 potassium oxalate	0	20	20	10
Method of timing.....	Slope of period of constant fall	Distance settled in 1 hour	Distance settled in 1 hour	Time to settle to 18 mm.	Graph of curve and distance settled in 1 hour
Sedimentation rate units.....	Millimeters per minute	Millimeters	Millimeters	Minutes	Slope of curve and millimeters
Correction for erythrocyte concentration	Required	Required	Seldom used	None	None
Normal range.....	0.05-0.40 mm. per min.	0-9 mm. men 0-15 mm. women	1-3 mm. men 4-7 mm. women	200-600 min.	"Horizontal line" and 2-8 mm. men 2-10 mm. women
Abnormal range					
Slight.....	0.4-0.6 mm. per min.	10-20 mm. men 20-25 mm. women	8-15 mm.	100-200 min.	"Diagonal line"
Moderate.....	0.6-1.0 mm. per min.	20-30 mm.	15-40 mm.	60-100 min.	"Diagonal curve"
Extreme.....	2.0-2.5 mm. per min.	35-50 mm.	80-110 mm.	15-30 min.	"Vertical curve"

For discussion of anticoagulants, see Ham, T. H., and Curtis, F. C.: Medicine **17**: 447 (Dec.) 1938.

* Dry oxalate mixture: The solution is made by dissolving 3 Gm. of crystalline ammonium oxalate and 2 Gm. of crystalline potassium oxalate in distilled water with the aid of heat, making the final volume to 100 cc. This gives an oxalate mixture concentration of 5 Gm. per hundred cubic centimeters. The concentration employed for blood is 200 mg. of oxalate mixture per hundred cubic centimeters of blood. Accordingly, 0.20 cc. of the solution is pipetted into a tube or bottle for each 5 cc. of blood to be drawn. The anticoagulant is then dried (to prevent dilution of blood) by heating in an oven at 100 C. for one hour or by desiccation at room temperature for several days. This anticoagulant has the advantage that it causes no change in erythrocyte size and no change in the sedimentation rate.

† Potassium oxalate: The solution is made by dissolving 20 Gm. of crystalline potassium oxalate in distilled water with the aid of heat, making the volume up to 100 cc. Concentration employed is 200 mg. per hundred cubic centimeters of blood. Accordingly, 0.05 cc. of solution is pipetted accurately for each 5 cc. of blood. This anticoagulant is not dried. It produces somewhat variable shrinkage of the erythrocytes, which can be corrected approximately by multiplying the erythrocyte volume (hematocrit reading) by the factor 108. This anticoagulant does not influence the sedimentation rate.

the plasma and serum globulins are not elevated above normal concentrations, but a normal sedimentation rate is not a reliable index for abnormally decreased concentrations of these globulins.

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SULFONE COMPOUNDS FOR PULMONARY TUBERCULOSIS

***To the Editor:*—Will you please send me information on the treatment of pulmonary tuberculosis with the sulfone drugs or any other effective drug therapy? Is there enough backing for a trial of sulfone compounds in a fairly severe case of tuberculosis with considerable loss of weight?**

L. E. Blachman, M.D., Cleveland Heights, Ohio.

ANSWER.—Feldman, Hinshaw and Moses were the first to employ in experimental tuberculosis a group of compounds known as sulfones. The nucleus of this group is 4,4′-diaminodiphenylsulfone. This parent compound has been found effective in controlling tuberculosis in animals, but, unfortunately, it is highly toxic. Therefore, various derivatives have been produced. Feldman and Hinshaw have employed not only the parent compound but ten derivatives in the treatment of experimental tuberculosis. Among these preparations five were found to have no significant effect, while the remaining six exerted varying good effects. The three which were found to be superior to all others are the parent compound and two derivatives, sodium p,p′-diaminodiphenylsulfone-N,N′-didextrose sulfonate (promin) and disodium formaldehyde sulfoxylate diaminodiphenylsulfone. The first of this group employed in experimental tuberculosis by Feldman and Hinshaw was the derivative commonly known as promin. They observed that, when this drug was administered a few days before animals were inoculated with tubercle bacilli, the expected course of the disease in these animals was materially altered; indeed, most of them were little effected by the disease. Animals were then infected with tubercle bacilli, after which the administration of the drug was begun at different periods. Indeed, in some animals treatment was not begun until six weeks after the usual lethal dose of tubercle bacilli had been administered. At the end of six months all of the control animals, that is, those which had been infected and were not treated with promin, were dead. Autopsy revealed the presence of severe widespread tuberculous lesions, whereas in 57 per cent of animals treated with promin it was impossible to find lesions in the liver, spleen or lungs. Moreover, those animals which were not treated until six weeks after they were infected fared as well as those treated earlier. The next experiment consisted in infecting guinea pigs with tubercle bacilli, later performing laparotomies in order to visualize the lesions and actually take specimens from the livers for microscopic examination. About this time treatment with promin was instituted. When all the untreated control animals in this study had died from tuberculosis, 81 per cent of those treated with promin were still alive. Necropsies on these animals revealed that not only had the disease failed to progress after the administration of promin but the lesions had receded and resolved. This is the first time in the history of tuberculosis therapy that tuberculosis in animals has been completely controlled by a drug.

Hinshaw, Pfuetze and Feldman have administered promin to 106 tuberculous patients. Thirty-six of these received what was regarded as an adequate trial of therapy. The most favorable effects were observed on exudative pulmonary lesions of recent origin without extensive destruction of tissue and without definite fibrosis. All such lesions showed evidence of improvement within two months and were nearly or completely resolved within four to six months. They emphasized the fact, however, that many such lesions tend to resolve spontaneously and that their series of cases is not large enough to justify the conclusion that promin was responsible for the observed improvement in the treated cases. Closure of one or more cavities was observed in 10 of 26 adequately treated patients with cavities, and tubercle bacilli apparently disappeared from the sputum in 14 of 36 cases (39 per cent). The sedimentation rate was definitely decreased in 70 per cent of all cases with elevated rate. Among 18 febrile patients 10 showed significant reduction in temperature. In 1 patient a new progressive lesion developed in the course of the treatment. Four patients died, 3 of whom were in the terminal stage before treatment was instituted. Six patients with tuberculous meningitis, 2 of whom had treatment instituted in an early phase of the disease, died. No noticeable effects were observed among 4 patients suffering from renal tuberculosis, but observations were incomplete in these instances.

The authors report that promin is potentially toxic when given in large doses; therefore the dose must be carefully regulated to avoid serious destruction of blood. Headache, restlessness, anorexia and malaise are the chief symptoms from which patients have complained. The authors are of the opinion that the results to date justify further clinical trial of promin and other drugs of the sulfone series, particularly among patients who have fresh exudative lesions. Under the direction of these workers a large number of patients are now being treated. Since the entire subject is in an experimental stage and since the drugs now in use are sufficiently toxic to result in serious harm to the patient, it seems best to refrain from prescribing these drugs until such time as their efficacy can be more definitely established and their dosage so standardized as to make their administration safe. No drugs of this series are available commercially at the present time.

Of all the other drugs that have been administered throughout the centuries, not one has been found efficacious in the treatment of tuberculosis in animals or man.

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"CANNED HEAT" FOR EMERGENCY USE

***To the Editor:*—Would you kindly inform me as to whether there is available a formula for a preparation of a substance such as the commercial "Sterno" for use in heat sterilization in the event of a situation in which gas and electricity should be unavailable?**

Shepard Shapiro, M.D., New York.

ANSWER.—Commercial preparations termed "canned heat" are jellies commonly containing denatured alcohol as a source of heat. A suitable formula, according to the Chemical Formulary by Bennett, volume I, 1933-1934, is denatured alcohol (methyl alcohol may be used) 1,000 cc., soap chips (well dried) 28-30 Gm., and shellac (dry flakes) 2 Gm. Heat the alcohol to 140 F. (Caution: Danger of fire), add soap chips and shellac, mix until the solids are completely dissolved, pour into suitable metal capped containers and allow to cool.

ROENTGEN THERAPY FOR RECURRENT HYPERTHYROIDISM

***To the Editor:*—The reply to a query on recurrent hyperthyroidism published in The Journal, Dec. 12, 1942, page 1262, surprised me in that the writer appears to feel that thyrotoxicosis is mainly a surgical problem. There is at present a useful nonsurgical treatment of diffuse thyroid enlargement associated with thyrotoxicosis which is the application of radium used as a collar over the neck by the method described in 1913 by Dr. Soloman Ginsberg. The consultant also stated in his reply that the skin may be burned, which is a misstatement that has been printed in every textbook on thyroid disease by those who write about it but who have had no experience with radiotherapy. I can conservatively state that at least 80 per cent of the diffuse swellings of the thyroid gland associated with thyrotoxicosis can be cured in this way. I am so enthusiastic about this form of treatment that I hold it comparable to the action of sulfonamide drugs in acute bacterial infections.**

Louis E. Weinberg, M.D., New York.